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ORIGINAL ARTICLES

MALE INFERTILITY—STATUS OF TREATMENT, PREVENTION, AND CURRENT RESEARCH 91
E. T. Tyler, M.D., Los Angeles, and H. O. Singher, Ph.D., Raritan, N. J.

TREATMENT OF MALE INFERTILITY WITH LARGE DOSES OF TESTOSTERONE 98
C. W. Charny, M.D., Philadelphia

REPORT OF PREGNANCIES IN INFERTILE COUPLES 102
W. C. Keettel, M.D., R. G. Bunge, M.D., J. T. Bradbury, Sc.D., and W. O. Nelson, Ph.D., Iowa City

MEDICAL OTOLARYNGOLOGY 105
F. W. Davison, M.D., Danville, Pa.

CONTROL OF POTENCY AND THE DOSAGE OF DIPHTHERIA AND TETANUS TOXOIDS 108
Louis Greenberg, Ph.D., Ottawa, Canada, and Rene Benoit, M.D., Montreal, Canada

PREVENTION OF RHEUMATIC FEVER BY TREATMENT OF PREVIOUS STREPTOCOCCIC INFECTIONS 114
Capt. A. J. Morris, Capt. Robert Chamovitz, (MC), U. S. A. F., Capt. F. J. Catanzaro (MC), Army of the United States, and C. H. Rammelkamp Jr., M.D., Cleveland

CLINICAL NOTES

RAPID TEST FOR ADRENOCORTICAL INSUFFICIENCY 117
Martin Perlmutter, M.D., Brooklyn, N. Y.

SPECIAL REPORTS

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES 118

EDITORIALS

Some Health Implications of the White House Conference on Education 120
Congress on Medical Education and Licensure 120

ORGANIZATION SECTION

The Journal Index 121
Michigan State Society Honors Los Angeles County Association 121

REGULAR DEPARTMENTS

Medical News 122
Meetings 126
Examinations and Licensure 128
Magazine-Television Report 128
Government Services: Air Force. Navy. Veterans Administration. Public Health Service 129
Deaths 130
Foreign Letters:
Austria: Electric Burns. Intraossal Phlebography. Bronchial Carcinoma 132
England: Influenza Vaccine Trials. General Practice in Scotland. New Antitumor Agent. Physician's Obligations 132
France: Irradiated Antirabic Vaccine. Hypothermia. Controlled Hepatectomy. New Hypotensive Agents 133
Italy: Congress of Stomatology. Vitamin E 133
Peru: Effect of Diuretics in Cirrhotic Patients. Award for Research in Bartonellosis. Acclimatization. Pyridoxine in Anesthesia 134
Sweden: Nobel Prize Winner, Professor Theorell. Mass Radiographic Examination of the Chest 134
Correspondence: Explosion Hazard During Anesthesia. International Medical Organizations. Diabetic Renal Complications 135
Business Practice: The Doctor Looks at Municipal Bonds 136
Woodward Burgert, M.D., Chicago
Medical Film Reviews 136
Medical Literature Abstracts 137
Book Reviews 150
Queries and Minor Notes: Leukemia Following Irradiation. Nasal Surgery Following Facial Injuries. Strongyloides Stercoralis Infestation. Recurring Sore Throat. Pelvic Tuberculosis. Immunity to Poliomyelitis Conferred to Infant. Ovulation Rare After Last Menstruation. Changes in Preserved Blood. Air Conditioner in Operating Room 151
Index to Vol. 159 ..... Follows page 152

WASHINGTON NEWS

The Opening of Congress. VA Reaction to Hoover Commission Recommendations. Report on Rate of Use of Poliomyelitis Vaccine. Grants for Research to Improve Hospital Services. Dr. Coggeshall to Succeed Dr. Keefer ..... Adv. Page 15
National Organizations of Medical Interest ..... Adv. Page 34
Tonics and Sedatives ..... Adv. Page 65
The Bright Side ..... Adv. Page 92
Books Received ..... Adv. Page 96
Index to Advertisers ..... Adv. Page 108

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MALE INFERTILITY—STATUS OF TREATMENT, PREVENTION AND CURRENT RESEARCH

Edward T. Tyler, M.D., Los Angeles
and
Heron O. Singher, Ph.D., Raritan, N. J.

• Evidence of impaired fertility in the male was found in nearly half of the infertile couples studied. Most of the infertile men were entirely normal as to body contours and other usual criteria of virility. No significant differences were found in a comparison of subfertile and azoospermic men with men of known fertility as to the fructose content of the semen and the urinary excretion of 17-ketosteroids. Paper chromatography revealed an unexplained difference between azoospermic men and the other two groups as to the distribution of amino acids in the seminal plasma. While in the cases of infertility the etiology in general was obscure, pregnancies followed in several instances of insemination with ejaculates concentrated by a special technique.

In the past decade there has been an upsurge of medical interest in the problem of male infertility. A major reason for this increased interest is the more generalized use of examinations for evaluating male fertility, with the resultant recognition that almost 50% of all sterile marriages may be attributable to the husband. In consequence, the clinical status of the infertile male merits current appraisal and an objective attempt to evaluate the accomplishments to date in this period of expanding medical knowledge. The survey presented here is based on our observations of 786 infertile couples, in clinic and private practice, of whom 358 (45.5%) showed impaired fertility or sterility on the part of the male.

GENERAL CHARACTERISTICS OF THE INFERTILE MALE

In discussing male infertility, it should be emphasized that the subfertile male is not, ordinarily, a "subvirile" male. Fertility is dependent upon production of spermatozoa within specialized testicular structures, the seminiferous tubules, whereas virility or "masculinity" is a result of many factors, including endocrine, which are unrelated to the basic ability to produce functional spermatozoa. In the average practice dealing with sterile males it is uncommon to find husbands with inadequacies in masculine characteristics of a significant degree. Most patients are entirely normal with regard to libido, development of the penis, body contours, hair distribution, and other criteria of good male endocrine effect. Sterile men who also exhibit marked endocrine hypogonadism are usually not clinical infertility problems, for many of them either do not marry at all or their marriages are based on prior acceptance of their barrenness.

In the search for more objective data on male hormone function of subfertile men, we employed certain laboratory studies that presumably are to some extent indicative of the degree of testicular endocrine activity. These included, specifically, determinations of 17-ketosteroid excretion and seminal fructose values. The quantity of urinary 17-ketosteroids is a measure, partially, of androgenic activity, for about one-third the amount excreted is said to be of testicular origin. Seminal fructose determinations have been suggested as an index of androgenic function, since the output of the seminal vesicles (from which all fructose in the semen is derived) is dependent upon male hormone stimulation. Table 1 presents seminal fructose and 17-ketosteroid findings in 30 "typical" normally fertile, subfertile, and completely sterile men. As may be noted, there were no marked differences in the values or average levels in the three groups. These findings support the clinical impression of the infrequency of endocrine hypogonadism among men who apply for treatment of fertility defects. A more complete evaluation of these studies has been reported elsewhere.[1]

From the University of California at Los Angeles School of Medicine (Dr. Tyler).
Read in the Symposium on Infertility Problems before the Section on Urology at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1955.
Certain biochemical studies reported herein were performed in the laboratories of the Ortho Research Foundation.
The betaine used in this study was supplied as Lipotaine by the Stuart Company, Pasadena, Calif. The gonadotropins were supplied by Lakeside Laboratories, Inc., Milwaukee.
1. Tyler, E. T.: Seminal Fructose Studies in Infertility, Fertil. & Steril. **6**: 247, 1955.

While emphasizing the differentiation between fertility and virility, reference should be made to the relatively uncommon syndrome of "fertile eunuchs," men who have good spermatogenic activity but who are physically eunuchoid. Such individuals, potentially capable of procreating, exhibit true organic impotence and present an entirely different problem. Patients of this type serve to further delineate the differences between actual reproductive ability and the popular concept of "masculinity."

"NORMAL" MALE FERTILITY

The question of what semen findings are compatible with normal fertility has been the subject of much controversy. About 10 years ago there was fairly general agreement that the average fertile male produced approximately 100 million spermatozoa per cubic centimeter, of which 85% were actively motile and normal morphologically in an ejaculate of 3 to 5 cc. Subsequently it was proposed that a sperm count level of 40 to 60 million per cubic centimeter should be considered normal, and this standard was accepted by the American Society for the Study of Sterility. In the past few years a further lowering of normal levels has been suggested, and MacLeod and Gold [2] believe that a sperm count of 20 million per cubic centimeter should be considered normal as long as motility is good.

TABLE 1.—*Comparison of Findings in Normally Fertile, Subfertile, and Azoospermic Men*

Group, Case No.	Seminal Fructose, Mg./100 Cc.	17-Ketosteroids
Normal		
1	412	18.6
2	180	17.2
3	390	16.5
4	395	19.0
5	586	10.2
6	0	14.5
7	608	9.6
8	192	11.0
9	386	9.2
10	412	12.6
Subfertile		
11	420	8.6
12	668	10.5
13	560	9.0
14	260	18.5
15	122	12.6
16	111	10.8
17	512	16.0
18	460	16.0
19	40	8.0
20	526	7.8
Sterile		
21	308	16.6
22	426	12.6
23	450	15.5
24	325	20.1
25	0	6.8
26	485	8.0
27	316	11.5
28	310	8.8
29	340	12.4
30	416	16.0

The establishment of a minimal normal fertile semen level is obviously more than an academic problem, for such standards provide an important guide to the extent of study and treatment required for the wife. Unfortunately, good statistical data for determination of normal fertility are difficult to obtain, a situation that adds to the present unsettled state of the problem. Thus, in the survey wherein semen specimens are examined from husbands whose wives are, or have been, pregnant, the specimen obtained may not necessarily be representative of the type that produced the conception. Some outstanding investigators, like MacLeod, have circumvented this to a considerable extent by examining repeated specimens when the initial one appears unusually low. This type of precaution increases the significance of such studies, but ordinarily it is difficult to get enough specimens from enough husbands, in instances where there is no sterility problem, to provide conclusive evidence of the adequacy of specimens with relatively low values. Other attempts, including our own, to establish standards for the male have involved data obtained on the frequency of conception in sterility patients in relation to the husbands' semen. This, too, exhibits a basic weakness, in that the couple as a "unit" is subfertile, and, while it may be assumed that the wife, in many instances, is normal, this cannot be readily accepted because of our incomplete knowledge of the factors that may reduce fertility in the female.

Another approach to the problem of establishing levels of normalcy involves obtaining information on the relative ease with which conception occurs when donor insemination is resorted to in instances where the husband's semen level is consistently low. One of us (E. T. T.) has analyzed such data utilizing cases of long-standing infertility in which spermatozoa counts as high as 25 million per cubic centimeter were obtained on occasion. Omitting instances of azoospermia, 23 pregnancies occurred with donor insemination of 37 patients.

Approximately 60% of the pregnancies occurred within three months when donor specimens were employed, even among those whose husbands had sperm counts often in the region of 20 million per cubic centimeter, with good grade and percentage of motility. This is the level that has been proposed as compatible with normal fertility. If such levels were actually normal, one could not expect pregnancy to occur so promptly with donor specimens. It can be argued that there are many known cases of conception occurring at extremely low sperm count levels. We, too, have observed such instances (apparently bona fide) but not commonly, and they are usually among young and presumably highly fertile wives, a situation of some significance, for it is fairly well accepted that a high degree of fertility in one mate can compensate for defects in the other. This may also explain the conceptions that occur when partners of a barren union each remarry and have children. It is our opinion that fathers with persistent sperm counts in the region of 20 million per cubic centimeter should not be considered normally fertile, but, rather, it should be assumed that their wives are more highly fertile than average. (A corollary of this is the implication that when the male is subfertile anything that can reasonably be done to increase the wife's fertility would merit trial.)

2. MacLeod, J., and Gold, R. Z.: The Male Factor in Fertility and Infertility: Semen Quality in Relation to Age and Sexual Activity, Fertil. & Steril. **4**: 194, 1953.

Russell,[3] in England, recently reported data of levels of normal male fertility based on repeated examination of semen of 72 men whose wives had had four or more successful pregnancies at short intervals. The lowest count among the 72 men was 53 million per cubic centimeter and in most instances was much higher. Four of the five men whose counts were below 60 million per cubic centimeter provided specimens at intervals of two weeks, and in no case did the count fall below 50 million per cubic centimeter. Such findings are at variance with those who believe that the critical sperm concentration

TABLE 2.—*Etiological Factors of Presumed Major Importance in 272 Subfertile and 86 "Sterile" Men*

Factor	Subfertile Group		"Sterile" Group	
	No.	%	No.	%
Cryptorchism (unilateral or bilateral)	19	7.0	9	10.5
Unilateral small testes	29	10.7	3	3.5
Bilateral small testes	61	22.4	28	32.5
Mumps atrophy (bilateral)	2	0.7	8	9.3
Mumps atrophy (unilateral)	10	3.7	1	1.2
Significant varicocele or hydrocele	33	12.1	..	....
Trauma atrophy (unilateral)	4	1.5	..	....
Gonorrhea	8	3.0	12	14.0
Toxic influences (specific)	2	0.7	..	....
Miscellaneous	12	4.4	3	3.5
Cause undetermined	92	33.8	22	25.5
Totals	272	100.0	86	100.0

is 20 million per cubic centimeter and that consequently the chance of fertilization does not improve if the count were above this level. These findings correlate with previous data reported by one of us (E. T. T.)[4] and would tend to support the contention that unless the husband repeatedly produces specimens above a 50 million per cubic centimeter level (other semen findings being relatively normal) he cannot be excluded from consideration in etiology of the couple's sterility problem.

CAUSES OF MALE INFERTILITY

While some husbands seeking treatment of infertility give histories of fairly obvious causative factors, the "average" patient is one in whom no clear-cut etiological picture is presented. In many instances the infertile husband has had little idea that his reproductive function is inadequate. This fact often is first made known to him after a period of marriage during which conception fails to occur and after which the wife's physician suggests that her husband be examined. A large number of these men are found to have bilaterally hypotrophic or atrophic testes. The fact that the testes are small is often not apparent to the patient, for it is surprising how many men with small glands believe that the size is normal. In some cases they may, of course, be confused by the size of the scrotum itself.

Bilateral small testes were found in 28 of the 86 sterile (azoospermic) men (32.5%) and 61 of the 272 relatively infertile men (22.4%) in this series, as indicated in table 2. Included in the table are the factors that we believed to be of major significance, although often a cause-and-effect relationship could only be conjectured. Gonorrhea was responsible for 12 cases of azoospermia (14%) but only 8 instances of reduced fertility (3%). Mumps was involved in 21 cases among both groups (5.8%), but this does not necessarily indicate the extent of its importance in sterility. There are several investigators who believe that testicular damage may occur from mumps, without evident orchitis, and that the seriousness of this disease is greater than has been generally recognized. No apparent etiological factors were present in 92 of the subfertile and 22 of the sterile men, a total of 114 of the entire group of 358 (31.7%). This relatively high percentage of cases of obscure etiology is a major obstacle to progress in the management of male infertility.

It will undoubtedly be necessary to resort to testicular biopsy much more often if we are to lower the percentage of "cause unknown" cases, but the biopsy data will need adequate correlation with detailed laboratory findings and history. Steps in this direction have already been taken by investigators such as Simmons [5] and Charny.[6]

TREATMENT OF MALE INFERTILITY

Since a large percentage of cases of male infertility are of obscure etiology, it may be anticipated that treatment would be highly unsatisfactory; experience has shown this to be the case. Table 3 summarizes the results obtained utilizing 984 courses of therapy in the present series of cases. Therapy used included thyroid, testosterone, various gonadotropins, liver and lipotropic substances, pregnenolone, methylandrostenediol, and diethylstilbestrol. Also evaluated are such measures as weight reduction, improvement in health habits, and prostatic massage. In analyzing therapeutic results, when one tries to eliminate the factor of spontaneous change by observing numerous specimens prior to, during, and after therapy, it becomes apparent that treatment, in general, is extremely unsatisfactory. Administration of lipotropic substances produced the best results, statistically, but

TABLE 3.—*Effects of Therapy in Subfertile Men*

Therapy	Total	Improved	
		No.	%
Thyroid *	156	21	13
Testosterone rebound †	36	3	8
Gonadotropins ‡	196	16	8
Liver and lipotropic substances §	201	30	15
General measures ‖	207	23	11
Miscellaneous steroids ¶	112	14	12
Prostatic massage #	76	5	7

* Extract administered orally to both subthyroid and euthyroid patients.
† Large doses of androgens for preliminary suppression.
‡ Including pregnant mare's serum, chorionic gonadotropins, bull and sheep pituitary extract, and combined gonadotropins.
§ Including betaine, methionine, choline.
‖ Including weight reduction and improved health habits.
¶ Including small doses of testosterone, pregnenolone, methylandrostenediol, diethylstilbestrol.
# 1 to 3 times weekly.

the percentage of improvement even here was only 14.9. In most instances, improvement was in the general region of 10%, a figure that is not high enough to exclude the importance of spontaneous change, with objective observation.

3. Russell, J. K.: Male Factors in Infertility, Reports of Societies, J. Obst. & Gynaec. Brit. Emp. **61**: 268, 1954.
4. Tyler, E. T.: Physiological and Clinical Aspects of Conception, J. A. M. A. **153**: 1351 (Dec. 12) 1953.
5. Simmons, F. A.: The Hypogonadal Male, editorial, Fertil. & Steril. **5**: 201, 1954.
6. Charny, C. W.; Conston, A. S., and Meranze, D. R.: Development of the Testes, Fertil. & Steril. **3**: 461, 1952.

Poor therapeutic results of this type make us question whether we are justified in subjecting infertile men to frequent "shots" or twice-weekly prostatic massages or in requiring them to use expensive medicaments. It would certainly seem injudicious to use the approach in which a single semen analysis is obtained, the patient placed on a regimen of two or three months' medication, and effects evaluated on the basis of a change of 5 to 10 million sperm per cubic centimeter in the subsequent specimen. Such changes, as a matter of fact, are often within the limits of errors in analyses, for the accepted accuracy of the sperm count is probably ± 10%.

It is our belief that virtually any therapy of male infertility today is completely experimental, and the physician employing it should do so only after relatively detailed study of the patient. While this may not contribute greatly to the success of therapy, it will help accumulate the type of evidence needed to predict the results that may be expected in given types of cases. In view of the lack of reasonably successful "medical" therapy for male infertility, various other approaches to the problem have been employed. A current one, utilized by one of us (E. T. T.), gives some hope of being effective in certain limited instances. This method of experimental treatment involves obtaining "partitioned" ejaculates from subfertile patients.

Partitioned Ejaculates.—It has been observed by many investigators that some husbands produce unusually large volumes of semen in which the sperm show poor concentration. The ejaculates of these men contain large total numbers of spermatozoa but in considerable dilution. Several patients in this series had semen findings in which the volume frequently ranged in the region of 10 cc., with total counts at times in the neighborhood of 200 million; yet their wives failed to conceive. Three such patients finally resorted to donor insemination, and each of the wives conceived, one within two months and the other two within four months. Cases of this type would seem to point out the importance of sperm concentration rather than total numbers in producing conception. (Experiments in lower animals have already furnished data of a similar nature.) Accordingly, certain current measures used in male infertility involve attempts to obtain more concentrated specimens without necessarily improving the total sperm count. Since it has been well established that the first portion of the ejaculate contains greater numbers of spermatozoa, one method of increasing sperm concentration involves the use of split ejaculates. The first third of the ejaculate contains approximately 75% of the spermatozoa, and, while it cannot be expected that ideal partitioning can be obtained clinically, it is surprising how well separation is often achieved. For some time we have used partitioned ejaculates for insemination, but unfortunately the results have not been encouraging. It is possible that the subnormal volume obtained when one uses a single split ejaculate is a factor that works against promoting fertility. For this reason we have more recently been obtaining several split ejaculates from the same patient, storing them, and utilizing them in frozen state as described below.

Frozen Semen.—Frozen semen (subsequently thawed) has been used in animal husbandry for several years. It has been well accepted that animals born as a result of conception produced by frozen semen show no significantly high rate of abnormalities, nor do several subsequent generations. Attempts at freezing human spermatozoa, and obtaining good survival following thawing, were not very successful until recently. In 1949, Parkes [7] in England, utilizing glycerol as a protective agent, was able to obtain fair sperm survival upon thawing several weeks after initial freezing. Subsequently Bunge and Sherman [8] were able to demonstrate that if large volumes were used better sperm survival was obtained with glycerol, and in 1953 these investigators reported successful pregnancies, with delivery of normal children, resulting from use of sperm that had been frozen and subsequently thawed. These evidences of the safety of frozen-thawed sperm have led us to attempt to obtain good "single" specimens by freezing the first portions of several split ejaculates and pooling them when thawed. The pooled specimen is then used for insemination at the wife's approximate ovulation time. In practice, the husband is requested to provide at least three or four specimens at intervals of about four days, preferably starting near the onset of the wife's menstrual period and ending about two weeks later. On the day of insemination an additional fresh partitioned ejaculate is obtained and the first portion added to the pooled thawed specimens.

The technique of freezing simply involves placing the first portion of the split ejaculate in a container after glycerol has been added in the proportion of 1 drop to 9 drops of semen. (The glycerol is dispersed in the semen by mixing with a rotating motion between the palms of the hands for about two or three minutes.) When the specimen is subsequently thawed it is best to place the vial in a water bath at room temperature, inasmuch as quick thawing appears to favor survival. One important requisite for obtaining maximal survival is to maintain as constant a temperature as possible in the dry-ice compartment. Observations on aliquots of the same specimen in containers in which changes of temperature are permitted to occur, compared to those in which good insulation and relatively constant temperatures are employed, demonstrate marked differences in survival rates.

In utilizing split ejaculates for storing and subsequent thawing, there have been two problems: 1. Many subfertile specimens show initial poor motility and subnormal morphology that inherently lower the total value of the subsequent pooled specimen. 2. Many oligospermic specimens with fairly good initial motility apparently do not tolerate the low temperatures as well as do normal specimens. Despite these facts, there are appreciable numbers of specimens that show good return of motility, particularly in the relatively short period of time required before utilizing them for insemination.

Thus far, three pregnancies have occurred among patients treated by this method. These were patients with long-standing infertility who had previously had many types of therapeutic procedures, one couple having been

7. Polge, C.; Smith, A. U., and Parkes, A. S.: Revival of Spermatazoa After Vitrification and Dehydration at Low Temperatures, Nature, London **164**: 666, 1949.

8. Bunge, R. G., and Sherman, J. K.: Frozen Human Semen, Fertil. & Steril. **5**: 193, 1954.

under continuous observation and treatment for two and one-half years. Single partitioned ejaculate insemination had been employed on all previously. The question of whether pooling the specimens was the factor enabling pregnancy to occur is unfortunately unanswerable, for the final addition of an unfrozen split ejaculate makes "controlled" observation difficult.

It is an unfortunate situation when one has to resort to this type of "mechanical" approach to a serious medical problem, but at the present time the usual methods appear to offer little hope of success. Until more basic information is obtained that will suggest specific lines of therapy for the inadequately functioning testes, these roundabout measures merit trial in selected instances. Certainly they have more physiological basis than barrages of expensive hormones and other drugs, whose lack of efficacy has been repeatedly and authoritatively reported.

PREVENTION OF MALE INFERTILITY

In view of the highly unsatisfactory state of therapy for male infertility, prevention is a matter of maximum importance. However, the problem of prevention seems to be as complex as the problem of treatment. One obvious reason for this is the fact, already mentioned, that so little is known about the most common etiological factors. It is quite difficult, ordinarily, to determine what particular trauma caused an end-result, found perhaps years later. Before much can be accomplished prophylactically, there are many questions to be answered: How many of the cases of "cause unknown" are actually instances of congenital defects? What common childhood illnesses produce damage to the testes undetected at the time? Are the somewhat common conditions like varicocele and hydrocele more serious, from the standpoint of damage to testes, than has been suspected? Information on these and other questions may help provide some appropriate measures for prevention.

Even certain obvious situations are often controversial, from the standpoint of preventing infertility. For example, it has long been believed that sterility can often be prevented by correcting cryptorchism. Cryptorchid testes are known to have what appears to be adequate hormone output, but they are defective in spermatogenesis. Recently, doubt has been cast on the belief that fertility can generally be preserved by bringing the testes into the scrotum. Charny [6] and others with extensive experience in surgery for cryptorchism now feel that, most of the time, the testes in cryptorchism are basically abnormal and that they will not function spermatogenically whether in the scrotum or not. Many physicians, however, believe that attempts should be made to bring down cryptorchid glands early in childhood, even prior to 2 years of age. In children this small it is best not to use much more than 250 I. U. of chorionic gonadotropin once or twice a week. Since many years of follow-up are required to determine the ultimate fate of treated cryptorchism, time and large series of carefully observed patients are obviously required.

An important consideration in preventing sterility is the avoidance of damage to reproductive structures during operations in the inguinal region. Even transient damage to the arteries supplying the testes may result in significant damage to spermatogenic function.

The relation of mumps to sterility is a matter of general recognition. However, there is disagreement as to the incidence of sterility caused by mumps. In the present series of 358 cases, definite information implicating mumps orchitis, etiologically, was obtainable in 21 (5.8%). The incidence of sterility due to mumps generally reported is considerably higher. It is believed that obvious orchitis may not necessarily be required for severe testicular damage to result. Stilbestrol is being utilized fairly extensively prophylactically for orchitis during mumps in adults, but the statistics are not as yet conclusive. There seems little to lose, though, in giving the small dose (1 or 2 mg. daily for a week) generally recommended. Prevention of the complications of gonorrhea has become fairly routine, with the widespread use of antibiotics. The low incidence of infertility of gonorrheal origin in our series and other recent series is a sign of effective current prophylaxis.

Other preventive measures have been suggested, such as maintenance of adequate protein intake and avoidance of even mild vitamin deficiencies, but the importance of these factors in the sterility problem is probably greatly overemphasized. Undoubtedly, the group of patients with atrophic or hypotrophic testes are the most profound problems. Obtaining adequate answers to many questions of etiology requires detailed attention to the genitalia on the part of those who treat children and adolescents. Information thereby obtained may help explain the end-results seen when the adult seeks aid, and, while the outlook is not good, it is possible that more may then be accomplished prophylactically.

BASIC RESEARCHES

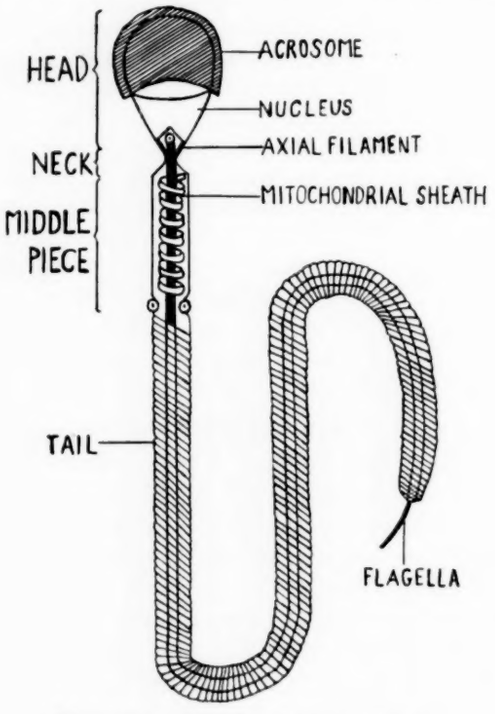
With the clinical problem of male infertility in an unsettled state, many physicians are looking to the laboratory for much-needed information. Studies are required on details, for example, of the maturation of the immature sperm cell and on the chemistry of the adult cell and the seminal plasma, as well as the relation of morphological sperm changes to fertilization potential.

Little is known about the chemical changes that occur during spermatogenesis; however, cytochemical studies have indicated that during the process of sperm maturation there are changes in the ribonucleic acid and desoxyribonucleic acid content of sperm cells. Along with these changes during development of the sperm cell, the alkaline and acid phosphatase of the nuclei decrease and glycogen disappears. Still another event is known to accompany the maturation of the sperm cell; namely, distinctive changes in the lipid distribution within the cell. These changes can be readily assessed by modern clinical laboratory techniques and may prove useful as methods of checking semen samples for the maturity of their cells or may be indicative of failures in the generative epithelium.

The major morphological features of the mature spermatozoon have been established during the course of the last century. As indicated in the figure, the sperm cell may be divided into head, neck, midpiece, and tail. The presence of the flagellum gives the human spermatozoon a filamentous form. The surface of this structure possesses high permeability, and this permits rapid response of the sperm cell to changes in the composition

of its environment. Thus, there results rapid equilibration with seminal plasma or cervical mucus or some synthetic mixture in which sperm are placed for preservation or spermicidal effect. These same filamentous structures probably explain the escape into seminal plasma of enzymes, such as hyaluronidase and cytochrome, without cell disruption.

The head of a sperm cell is filled mainly with the nucleus, which is for the most part composed of desoxyribonucleic acid and its associated proteins. The cell as a whole is covered by an outer sperm membrane consisting of keratin-like lipoproteins. The strength of this membrane varies considerably from species to species and probably accounts to some extent for differences in their resistance to lytic agents. There are also a large number of enzymes that have been demonstrated to be in the cell, but their exact cytological locus has not been



Schematic representation of a spermatozoon.

established; these are the enzymes of the glycolytic system, which may be part of the system for supplying the energy of motion, and hyaluronidase, which is evidently essential to enable the spermatozoon to penetrate the cumulus cell mass that surrounds the unfertilized egg. Absence or lack of key components of the glycolytic system may explain rapid loss of motility or ability to effect fertilization in otherwise normal semen.

To date, none of these morphological or biochemical discoveries has led to an understanding of infertility, but they have emphasized the complexity of the structure and underlined the interdependence of the various systems that must be in balance in the normal spermatozoa. They have exemplified possible mechanisms by which failure of the germinal epithelium may be evaluated.

Besides sperm, the other component of semen, seminal plasma, represents a composite mixture of fluids secreted by the epididymidis, the vas deferens, ampulla, prostate, seminal vesicles, Cowper's glands, and perhaps others. These help account for the complexity of this fluid. In man, the secretion of the prostate is the major source of the seminal plasma citric acid and acid phosphatase. Determination of level of these elements is an indication of the functional state of the prostate gland.

The seminal vesicles, as previously noted, constitute the main source of reducing sugar, fructose, for the seminal plasma. In species other than man, a powerful sulfhydryl-containing reducing substance, ergothioneine, has been demonstrated and probably acts as a protective substance, as mentioned by MacLeod.[9] In man this sperm-protective role is taken over by ascorbic acid and other as yet unidentified materials. It is well within the limits of probability that perfectly normal sperm may be "poisoned" by components of the seminal plasma. These enzyme "poisons" or inhibitors might be preformed or result from events that occur after ejaculation. Some attempts have been made to evaluate these potentialities clinically, but more widespread use of seminal plasma effects on "metabolic criteria" of normal sperm would appear to be needed.

Besides these constituents, whose source is known, seminal plasma contains a large number of other components of unknown origin; among these are phosphorylcholine, spermine, and free amino acids. Phosphorylcholine may be related to lipid metabolism; spermine may function as a bacteriostatic agent. Several amino acids have been shown to prolong sperm viability in lower forms in various studies by A. Tyler. The free amino acids have been studied in relation to infertility by one of us (H. O. S.) with the techniques of paper chromatography using fresh specimens as well as subfertile specimens shipped cross country in frozen state and subsequently thawed. Paper chromatography is the separation of a mixture of amino acids, the basic building stones of proteins, on filter paper by means of solvent transport. The amino acid mixture is placed on one spot on the paper, and solvent is then passed through the paper in a given direction by capillary attraction. The solvent carries the amino acids with it, different amino acids traveling at different rates, resulting in separation. Chromatographically, a unit Rf is defined that represents the distance a given component has moved divided by the distance the solvent itself has moved. Under fixed conditions Rf values can be identified with specific amino acids.

The cases considered (table 4) have arbitrarily been divided into groups showing zero sperm counts, counts up to 10 million per cubic centimeter, and those possessing over 10 million sperm per cubic centimeter. In groups possessing Rf values 0.0-0.23, 0.25-0.29, 0.36-0.45, 0.56-1.0, all of the samples appeared to possess the amino acids to the same extent. In the group possessing Rf values 0.24-0.25 and 0.33-0.35, the specimens with sperm counts of 0 to 10 million and more than 10 million show the same incidence of samples within this group. In the group that have zero sperm, these Rf groups occur almost twice as frequently. In the groups of amino acids possessing Rf values 0.3-0.33 and 0.51-0.55, the incidence is reversed; that is, the zero sperm count group possesses a lower incidence of these amino

9. MacLeod, J., in Engle, E. T.: The Problem of Fertility, Princeton, N. J., Princeton Press, 1946, p. 154.

acids groups. While these differences have been observed, it is difficult to ascertain why variations in sperm concentration should affect the plasma.

Besides these constituents of relatively simple structure, seminal plasma also contains proteins of enzymatic and nonenzymatic nature. Besides the phosphatases contributed by the accessory glands, the plasma also contains the precursor of a fibrinolytic enzyme and at least two proteolytic enzymes. The liquefaction of human semen, after coagulation, is probably a result of the action of these enzymes. It may also be possible that the enhanced viscosity of some samples may be the result of an increased concentration of nonglobular proteins and a relative decrease of enzymatic activity.

Among the other proteins of seminal plasma that possess physiological activity are those that produce a stimulation of isolated smooth muscle strips, such as that of

TABLE 4.—*Amino Acid Distribution in Seminal Plasma*

Rf *	Amino Acids Included in Group	Sperm Count, Millions/Cc. 0	0-10	Over 10
	Total no. of samples.....	75	68	134
0.24-0.25	Lysine	54	34	37
0.30-0.33	Arginine	25	55	53
0.33-0.35	Cystine, glycine	44	24	29
0.46-0.50	Aspartic acid, serine, glutamic acid	67	65	81
0.51-0.55	Alanine, threonine, proline	27	43	43

* Distance a given component has moved divided by distance the solvent itself has moved.

the uterus, and a pressor action on blood vessels. Von Euler [10] demonstrated the presence of choline and two substances that he named prostaglandin and vesiglandin in seminal plasma that affected the contraction of the smooth muscle.

Extension of the study of the physiological effects of seminal plasma components on the excised strips of uterine musculature has revealed the existence of several components of both proteinaceous and nonproteinaceous nature that can elicit this response. Low temperature alcohol fractions of seminal plasma have revealed at least two proteins that will produce contraction in the smooth muscle strip and perhaps a third that is inhibitory. Of the nonprotein components, there is at least one noncholine material (prostaglandin?) that will induce similar changes. There has been no attempt in our series of experiments to correlate any qualitative relationship between the ability of seminal plasma to induce contraction in the excised strip and the fertility of the semen. The in vivo effect of adding these active elements to semen samples of low fertility has not yet been evaluated.

The physiological significance of these materials in reproduction is unknown, but various regulatory actions have been attributed to them. Thus, they have been thought to be the agents that control the voiding of the secretions of the prostate and seminal vesicles, or they may have a pharmacodynamic influence upon the smooth musculature of the female reproductive tract. However, in vivo experimental data proving or disproving any of these assumptions are still lacking. There are also components of seminal plasma that act like epinephrine in that they raise blood pressure and increase respiration. No essential role in reproductive physiology is known for these materials.

Chemical and biochemical investigations have, as yet, certainly not explained or unraveled the complexities of male infertility. However, they have introduced several new methods of approach to an understanding of some of the intricate mechanisms that underlie sperm motility, and they may develop some "guide lines" to possible diagnosis of potential sites of "failure" in the patient.

COMMENT

In a period during which many strides have been made in various fields of medical practice, progress in the prevention and treatment of male infertility has been comparatively slow. There are still great deficiencies in information concerning the standards of normal fertility. It can only be conjectured, but not fully understood, why some husbands with apparently low seminal values are able to impregnate their wives while others with similar semen findings are not. Adequate data, moreover, have not been obtained to provide even a clue to the answer of such questions, for example, as the relation of abnormal sperm morphology to miscarriage. These and other problems require a great deal more attention than they have been given. Estimates that as high as 10% of marriages in this country are involuntarily barren would indicate that infertility may affect as many as 5 million people. Certainly no phase of medicine merits more profound study than that which relates to one of the most basic human needs—the need to reproduce. It is our earnest hope that in the next decade research organizations will give the type of impetus to laboratory and clinical studies of infertility that has been given to problems of lesser magnitude in the past.

SUMMARY

The problem of treating male infertility has become of increasing clinical importance as a result of the more generally recognized fact that the husband is often responsible for lack of conception. In our series of 786 couples, 358 (45.5%) showed evidence of reduced fertility on the part of the male. Most infertile husbands are entirely normal from the standpoint of masculine characteristics. Etiological factors are not evident in a high percentage of cases. Approximately one-third of the patients fall into a category of "cause unknown," while a similar number show bilaterally small testes, often of obscure etiology.

Arbitrary standards for male fertility are difficult to establish. Medicinal therapy for the infertile male is relatively disappointing. The patient's spermatogenic function may be utilized to possible greater advantage by pooling frozen-thawed partitioned ejaculates, in certain instances.

Laboratory research studies have shown differences in amino acid composition of semen of varying levels of fertility but fail to shed much light on the basic deficiencies, other than those routinely observed, in subfertile semen specimens. In experiments with semen fractions, certain components have been demonstrated to have stimulating effects on uterine muscle, a finding that theoretically may have clinical significance.

10911 Weyburn Ave. (24) (Dr. Tyler).

10. Von Euler, U. S.: Pharmacodynamic Effects of Prostaglandin, Nord. med. **42**: 1463, 1949.

TREATMENT OF MALE INFERTILITY WITH LARGE DOSES OF TESTOSTERONE

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• ***The administration of a standard course of testosterone in a series of subfertile male patients resulted, as a rule, in the disappearance of spermatozoa from the semen after 12 weeks. After termination of this treatment, spermatozoa reappeared in two or three months. While in some cases the sperm counts returned to the pretreatment level, in others they failed to reach it during the period of observation and in some they exceeded it (rebound phenomenon).***

The selection of patients must be governed by determinations of urinary gonadotropin excretion and by testicular biopsy, especially the latter. In one initially azoospermic patient the rebound phenomenon was observed twice and a peak count of 30 million spermatozoa per cubic centimeter was achieved. In this instance a pregnancy followed, with subsequent normal childbirth.

It has long been known that the administration of a gland extract to an experimental animal serves to depress the function of the gland from which the extract originated. In 1938, applying this principle to the testis, Hamilton and Leonard,[1] Moore and Price,[2] and Zuckerman [3] found a reduction of testis weight and a depression of spermatogenesis in experimental animals treated with large doses of testosterone. This effect of testosterone was probably mediated through inhibition of the anterior pituitary gland.

In men, McCullagh and McGurl [4] reported a drop in sperm count "followed by a rise while treatment was in progress, but in no case did the rise reach the original high level found prior to treatment." In 1951 Heckel [5] observed a "temporary depletion of spermatozoa" in 10 of 12 men treated with testosterone for prostatic hypertrophy. The first report on the use of large doses of testosterone in male infertility appeared in 1950. Heller and co-workers [6] reported the results of testosterone administration, employing 25 mg. daily for from 24 to 29 consecutive days in a series of 20 men. A statistical analysis of their patients was not given, but they reported marked improvement in spermatogenesis as judged by biopsies before and after treatment. They advised the use of this mode of therapy in "infertile men having elevated gonadotrophins and hyalinization of the membranes of the seminiferous tubules accompanied by marked germinal defects."

Heckel and his co-workers [7] have issued several reports on infertile men treated with testosterone. Biopsies were not done routinely prior to treatment, and gonadotropin and ketosteroid excretion determinations were not made in many of their cases. Their results, however, were more encouraging than those of Heller. In 1952, they reported a series of 36 men who had completed treatment, 23 of whom showed improvement. Werner [8] observed spermatogenesis in an eunuchoid man in the 11th year of androgen therapy and quoted others with similar experiences. He believed that it was an instance of the rebound phenomenon occurring after prolonged testosterone administration.

Several reports [9] appeared on the results of intratesticular inclusion of testosterone crystals or pellets, and many observers have reported improvement of fertility with small doses of the hormone administered intramuscularly. In these instances, however, the stimulation allegedly occurred during the period of absorption of the testosterone and was not a rebound phenomenon.

At the 10th annual meeting of the American Society for the Study of Sterility, in June, 1954, Heller presented a series of 103 cases, in which 19% showed improvement. MacDonald reported 106 cases (in 80 of which biopsies were done), with 21% showing improvement. Getsoff, reporting on 450 questionnaires, analyzed the replies from 104 doctors, of whom 64 stated that they had employed large doses of testosterone in male infertility. From the questionnaires, he accumulated a total of 840 cases, in only 60 of which were testicular biopsies done as a control. Sixty-three of the 840 patients (7.5%) were allegedly improved.

Some conservative clinicians have decried the issuance of reports that they consider premature. They justifiably caution against widespread, indiscriminate, uncontrolled use of a potent agent because of their own experiences. The latter include instances of permanent spermatogenic depression, resulting in the conversion of infertile males to absolutely sterile ones. They

From the Albert Einstein Medical Center, Southern Division.

Read in the Symposium on Infertility Problems before the Section on Urology at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1955.

1. Hamilton, J. B., and Leonard, S. L.: The Effect of Male Hormone Substance upon the Testes and upon Spermatogenesis, Anat. Rec. **71**: 105, 1938.

2. Moore, C. R., and Price, D.: Some Effects of Testosterone and Testosterone-Propionate in the Rat, Anat. Rec. **71**: 59, 1938.

3. Zuckerman, S.: The Effect of Testosterone Propionate on Testicular Function in Monkeys, Lancet **1**: 1162, 1938.

4. McCullagh, E. P., and McGurl, F. J.: Further Observations on the Clinical Use of Testosterone Propionate, J. Urol. **42**: 1265, 1939.

5. Heckel, N. J.: Spermatogenic Rebound in Human Following Administration of Testosterone Propionate, A. M. A. Arch. Surg. **63**: 4 (July) 1951.

6. Heller, C. G., and others: The Effect of Testosterone Administration upon the Human Testis, abstracted, J. Clin. Endocrinol. **10**: 816, 1950.

7. Heckel, N. J.; Rosso, W. A., and Kestel, L.: Spermatogenic Rebound Phenomenon After Administration of Testosterone Propionate, J. Clin. Endocrinol. **11**: 235, 1951. Heckel, N. J., and MacDonald, J. H.: Rebound Phenomenon of Spermatogenic Activity of Human Testis Following Administration of Testosterone Propionate: Further Observations, Fertil. & Steril. **3**: 49, 1952.

8. Werner, S. C.: Spermatogenesis and Apparent Fertility in Eunuchoid Male in 11th Year of Androgen Therapy, J. Clin. Endocrinol. **11**: 612, 1951.

9. Swyer, G. I. M.: Effects of Testosterone Implants in Men with Defective Spermatogenesis, Brit. M. J. **2**: 1080, 1953. Schuermann, H.: Intratestale Androgenapplikation bei schweren Fertilitätsstörungen, Klin. Wchnschr. **29**: 201, 1951. Ezes, H.: Base, résultats et indications du traitement de certaines insuffisances spermatiques par la testostérone in situ, Ann. endocrinol. **13**: 90, 1952; Restauration de la spermatogénèse chez le lapin par inclusion testiculaire de cristaux de testostérone, ibid. **11**: 78, 1950. Trabucco, A., and Botinni, E. B.: Acción de la testosterona sobre la espermatogenesis (consideraciones sobre siete casos clínicos), Obst. y ginec. latino-am. **7**: 611, 1949. Ragab, A. F.: Treatment of Oligospermia with Testosterone Propionate, J. Roy. Egyptian M. A. **34**: 390, 1951.

deplore the administration of large doses of testosterone that will temporarily and perhaps permanently depress spermatogenesis unless the patients are under the care of clinicians who have facilities for continuous laboratory control.

My own series consists of 152 infertile males, only 92 of whom are analyzed here. The data on the remaining 60 are incomplete because either they failed to return for sufficient follow-up or the period of observation following testosterone withdrawal is still too brief. It might be noted here that four of the patients not included because of "lack of cooperation" failed to return because of their wives' intervening pregnancy. They are nevertheless not included in this analysis, because there is no proof of semen improvement.

In the 92 patients herein analyzed, the pretreatment sperm counts were as follows: azoospermia, 9; below 5 million per cubic centimeter, 36; 5 to 10 million, 29; and 10 to 20 million, 18. All of the patients had testicular biopsies, as well as urinary gonadotropin and 17-ketosteroid determinations prior to treatment. The biopsy was used as a guide, in that patients were excluded from any type of treatment if the biopsy revealed either absence of germinal epithelium or so much fibrosis and shrinkage of the seminiferous tubules that regeneration was considered unlikely. Patients were considered suitable for treatment if their biopsies revealed arrested development at any stage (spermatogonium, spermatocyte, or spermatid), especially if premature desquamation of the epithelium into the lumen of the tubule was noted. The gonadotropin determination was used as a guide, in that only patients with high or normal gonadotropin excretion were treated with testosterone. Patients who had hypogonadism secondary to pituitary hypofunction were treated with chorionic gonadotropins and are not included in this survey.

Forty patients, including the nine with azoospermia, received 75 mg. of testosterone intramuscularly twice weekly for 18 weeks, a total of 2,700 mg. Fifty-two patients were given 200 mg. of repository testosterone intramuscularly once weekly for 15 weeks, a total of 3,000 mg. Semen examinations were made at frequent intervals during the course of treatment. The administration of testosterone was not stopped as soon as spermatozoa disappeared from the ejaculate but was continued until the full dosage had been given.

SEMEN EXAMINATIONS

Prior to treatment, two or more examinations were made. If the testicular biopsy revealed a picture at variance with the semen reports, additional examinations were done in order to check on the accuracy of the previous tests. During the period of treatment, semen examinations were done every six weeks. Generally the third examination was made immediately after the last dose of testosterone had been given. After the withdrawal of testosterone, examinations were done at monthly intervals.

RESULTS

Production of Azoospermia.—As a rule spermatozoa disappeared from the semen after 12 weeks (1,800 mg.) of testosterone administration. This was especially true in those patients whose initial sperm counts were below 5 million per cubic centimeter. The injections were nevertheless, as stated previously, continued for an additional six weeks (900 mg.) in all instances. It was not necessary to give any patient more than 2,700 mg. in order to produce azoospermia.

Rebound Phenomenon.—In most patients spermatozoa first reappeared in the semen three months after testosterone withdrawal, although in a few instances some spermatozoa were found after two months. Once present, the increase usually continued through the fourth and fifth months, at which time a peak was reached. In only an occasional patient was the rise in sperm count continued beyond this point. In many of the unsuccessful cases the sperm count rose to pretreatment level three months after testosterone withdrawal and remained unaltered for the remainder of the period of observation. In a few patients the sperm count rose slightly but not appreciably during the fourth month but

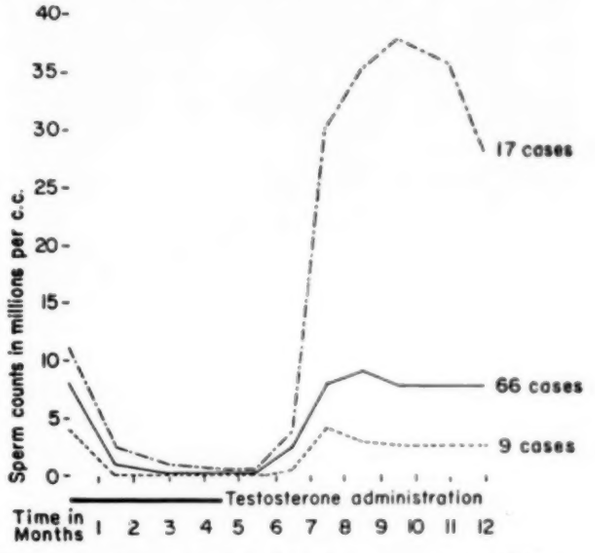

Fig. 1.—The three types of rebound response after withdrawal of testosterone are shown by the curves, which represent composite results.

then dropped to the pretreatment level on the next examination. In patients made worse by the testosterone, the sperm count did not rise to the pretreatment level.

Evaluation of the results was difficult in patients whose pretreatment sperm counts were over 10 million per cubic centimeter. When the periodic variations in semen picture were considered, a post-treatment increase in sperm population of as much as 50% had to be judged with caution. Only those patients are listed in the improved column whose sperm counts were consistently increased, following the pattern previously described. The curves in figure 1 represent composite pictures of progress in the three types discussed.

Azoospermia.—Nine patients with azoospermia were treated. All had biopsies displaying "reversible" lesions, that is, a relatively uniform histological picture revealing some progress in spermatogenesis and a minimum of fibrosis. In these, premature desquamation of the seminiferous epithelium constituted a favorable prognosis. Each of the nine patients received a total of 2,700 mg. testosterone during a period of 18 weeks. The treatment was a failure in seven of these nine patients; no spermatozoa appeared at any time.

One patient was classified as improved, inasmuch as spermatozoa appeared three months after testosterone withdrawal. After four months his sperm count was 2,800,000 per cubic centimeter; after five months 3,700,000; and after six months 2,200,000. It remained

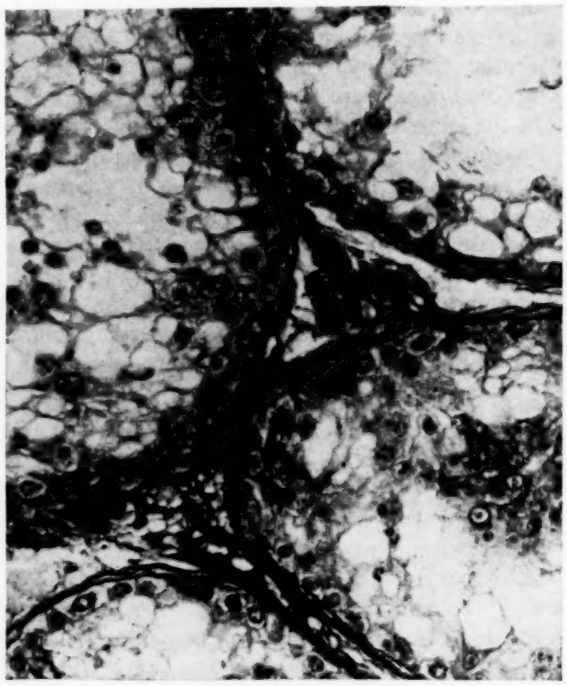

Fig. 2.—Biopsy specimen of testis before treatment. Spermatogonia and some spermatocytes are present. Note the premature desquamation of seminiferous epithelium (× 250).

at about that figure for the remaining 16 months of the period of observation. The progress of the remaining patient is described in the following case report.

REPORT OF A CASE

A 29-year-old man was first examined on Oct. 4, 1952. He had matured sexually at age 16 to 17. He had been married for two and one-half years and had never used contraceptives. He was somewhat undernourished, being 5 ft. 7 in. tall and weighing 120 lb. (54.5 kg.). The upper and lower measurements were equal. The hair distribution was normal. The scrotum was small, but the testes were normal in size and consistency. The prostate gland was palpably normal, and its secretion was free of infection. Urinary excretion of gonadotropin was 4.5 Rubin units in 24 hours and of 17-ketosteroid was 19 mg. The semen was azoospermic on three examinations. There was an average of three epithelial cells per high-power field, which could not be accurately identified but which were believed to have originated in the seminiferous tubules. Testicular biopsy disclosed arrested development of spermatogenesis, with considerable desquamation of the epithelium. Most of the tubules contained spermatogonia only; a few disclosed development up to the primary spermatocyte stage, and still a smaller number of tubules contained secondary spermatocytes. Only an occasional tubule had spermatids within its lumen. The Sertoli cells were normal. The peritubular tissue disclosed no fibrosis, and the interstitial cells of Leydig were normal in appearance (fig. 2).

The administration of testosterone was begun on Oct. 26, 1952, and was continued twice weekly without interruption until Feb. 2, 1953, for a total of 36 injections (2,700 mg.). Semen examinations on March 23 and April 20 revealed azoospermia. Spermatozoa appeared first in the specimen of May 20, three months after testosterone withdrawal. Their number continued to increase for the next two months, reaching a maximum of 11,400,000 per cubic centimeter, and then declined. Testicular biopsy on June 23, four months after testosterone withdrawal, revealed unmistakable improvement of the histological picture. Many of the tubules disclosed normal spermatogenic activity. Even those that did not display complete development showed marked evidence of stimulation. Primary and secondary spermatocytes were present in almost all of the tubules. The interstitial cells of Leydig remained unaltered (fig. 3). (Figure 4 illustrates the patient's entire course.)

On Oct. 29, 8 months after testosterone withdrawal, the patient's sperm count had declined to 2,400,000 per cubic centimeter, and a second course of testosterone was instituted and continued for 18 weeks (2,700 mg.), even though azoospermia was noted after 12 injections (900 mg.). Three months after withdrawal of the testosterone, on June 26, 1954, semen examination revealed a volume of 3.8 cc. and a sperm count of 12 million, with 40% motile spermatozoa in the fresh specimen. One month later, on July 30, the volume was 6.0 cc. and the sperm count 30,400,000, with 50% motility. On Aug. 23, the volume was 7.0 cc. and the count 24 million, with 60% motile spermatozoa. On Sept. 18 the volume was 6.5 cc. and the count 19,600,000, with 50% motility. On Oct. 30 the volume was 9.0 cc., but the sperm count had fallen to 9,200,000, and, on Jan. 6, 1955, it had dropped to 4,400,000 per cubic centimeter. However the patient's wife had missed her August menstrual period, and, on Sept. 15, 1954, pregnancy was diagnosed. The pregnancy was terminated with the birth of a son on April 28, 1955.

COMMENT

The results of treatment in this series are shown in the table. An improvement of only 18% of treated patients does not, at first glance, appear to be a noteworthy step in therapy. Yet, when one considers that most of

Results of Treatment with Testosterone in Ninety-Two Infertile Men

Pretreatment Sperm Count, Million/Cc.	No. of Patients	Improved		Not Improved		Made Worse	
		No.	%	No.	%	No.	%
Azoospermia	9	2	22.2	7	77.8	..	....
0- 5	36	5	13.8	25	69.5	6	16.7
5-10	29	5	17.2	22	75.8	2	7.0
10-20	18	5	27.7	12	66.7	1	5.6
Totals	92	17	18.5	66	71.7	9	9.8

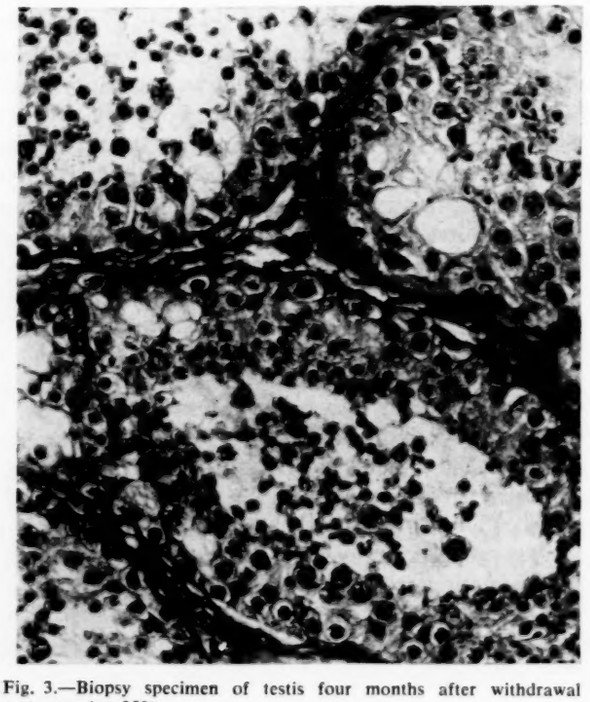

Fig. 3.—Biopsy specimen of testis four months after withdrawal of testosterone (× 250).

these men had either been previously treated unsuccessfully or had been excluded from treatment because none was available, the salvage of even such a small number

becomes impressive. It is only fair to concede that this method of treatment is merely a temporary phase in the management of the infertile male. When the intricacies of the mechanism of the rebound phenomenon have been unfolded, a more direct method of stimulating spermatogenesis should be available. In compiling the statistics listed in the table, I gave every consideration to the fact that there is considerable spontaneous variation in sperm counts of fertile and infertile men. Fertility was not considered improved unless the increase in sperm population was at least 50% above the pretreatment level and followed the pattern and timetable already described.

To those who would object to the inclusion of even such cases in the "improved" category, the two patients with initial azoospermia whose ejaculates contained spermatozoa three months after the withdrawal of the testosterone should serve as unquestioned evidence of the beneficial effect of the treatment. Even more significant is the evidence presented in the detailed history of the patient who received two courses of testosterone and who "rebounded" after each course. The appearance of actively motile spermatozoa three months after the termination of the first course of testosterone and their reappearance in even larger numbers after the second course of testosterone should be sufficient to convince even the most skeptical observers. The improvement of spermatogenesis as demonstrated by testicular biopsies taken before treatment and at the height of the first rebound is further proof of the stimulation afforded by the treatment.

It might be worth noting that the progressive rise in sperm counts during a period of a year or more, as reported by Heller and by Heckel and MacDonald, was not observed in these patients. In this series, the sperm count rose to its maximum from three to five months following withdrawal of the testosterone and, in most of the cases, began then to decline toward the pretreatment level. Where pregnancy intervened (5 out of the 17 improved cases), it occurred within five or six months of hormone withdrawal. Another point favoring the use of large doses of androgens is that in many of the unimproved cases, a second biopsy, performed three months after testosterone withdrawal, revealed more active spermatogenesis even though the number of spermatozoa in the ejaculate was not appreciably increased. In other words, the stimulus was sufficient to affect favorably some phases of spermatogenesis, such as spermatocyte division, but not enough to extend to spermatozoal maturation.

The selection of patients for treatment with large doses of testosterone was governed by two important diagnostic aids: testicular biopsy and urinary excretion of gonadotropins. The information obtained by testicular biopsy has been most important. Only those patients who had reversible lesions were considered favorable candidates. A lesion was considered reversible if the tubules were normal in size, presenting either absence or a minimal degree of sclerosis, and contained Sertoli cells and spermatogonia within the lumen. Premature desquamation of seminiferous epithelium was also considered a favorable prognostic sign. The amount of gonadotropin excreted in a 24-hour period was also used as an index, patients having low outputs being excluded from treatment. Those with normal or high gonadotropin excretion were considered favorable candidates.

The optimum dosage of testosterone has still to be determined. In this series a uniform dose was given to each patient without regard to his weight or to the initial semen picture. The total amount of androgen administered to men with initially low counts was greater in this series than that given by Heller and by Heckel and MacDonald. Although, in many instances, 1,800 mg. of testosterone was sufficient to produce azoospermia, its administration was continued for six weeks more (900 mg.). The use of repository testosterone, 200 mg. once weekly for 12 weeks, appeared as effective in producing azoospermia and subsequent rebound as testosterone propionate administered in doses of 75 mg. twice weekly for 18 weeks. It is possible of course, that an even smaller quantity of testosterone, less than that necessary to produce azoospermia, would produce a more effective rebound.

The increased sperm count in the patient who received a second course of testosterone after the first had been partially and temporarily effective deserves special consideration. Two possible inferences can be drawn from this experience: 1. The initial dose of 2,700 mg. of testosterone sufficed only to produce a moderate rebound; larger amounts should have been administered. 2. The mechanism of the rebound is such that intermittent administration of testosterone is a more satisfactory method of treatment. It is important to emphasize that this mode of treatment is applicable in only a limited number of patients with infertility problems; that it should be preceded by a careful and complete survey of the patient; and that its indiscriminate use will serve only to discredit it.

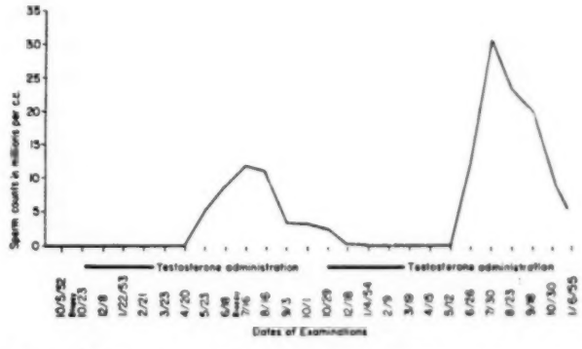

Fig. 4.—Course of the patient who had a favorable response to two courses of testosterone.

SUMMARY

Complete treatment of 92 infertile males by means of 2,400 to 2,700 mg. of testosterone during a 12 to 18 week period yielded an over-all improvement in 18.5%. Spermatozoa appeared in the ejaculates of two initially azoospermic patients. The future of testosterone therapy is still uncertain. When the mechanism of the rebound phenomenon is better understood, a more direct method of stimulating spermatogenesis will be available.

2039 Delancey Pl. (3).

REPORT OF PREGNANCIES IN INFERTILE COUPLES

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and
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• In the infertile women the most frequent findings were menstrual irregularity and endometriosis. In the men, examination of the semen revealed azoospermia in more than an eighth of the cases studied. Instances of nonliquefying semen were found, but insemination with material liquefied by alpha-amylase was not followed by conceptions.

The treatment of infertility was more successful in the cases that involved the female partner. In some instance pregnancy followed shortly after tubal insufflation, but a causal relationship could not be proved. Conceptions followed artificial insemination with either fresh or frozen material. The frequency of obstetric complications was not increased above the usual figures in this series.

There have been numerous articles published concerning the value of the various diagnostic methods and therapeutic procedures available in the management of male and female infertility. However, only a few publications are concerned with the pregnancies achieved and the therapeutic procedures proved most valuable. In their reports the authors often were overly enthusiastic about a given procedure considered responsible for the pregnancy. Therefore, it seemed timely to review the pregnancies accomplished in our infertile patients in order to determine the procedures considered of therapeutic value and those that were related to time or chance.

ORGANIZATION

Prior to January, 1952, both male and female infertility patients were seen in the department of obstetrics and gynecology, State University of Iowa Hospitals, and were interviewed and examined by individual physicians. Gradually it became apparent that the sterility investigations were not thorough enough, so an association of interested and qualified individuals was organized to study these problems. Fortunately, a congenial professional association led to this cooperative investigative effort. The group consisted of a urologist (R. G. B.); an anatomist (W. O. N.), who interpreted the testicular biopsies; a gynecologist (W. C. K.); and an endocrinologist (J. T. B), who conducted hormone assays and interpreted the endometrial biopsies. At weekly conferences, the clinical histories and findings were presented and further diagnostic studies or therapeutic measures were recommended. A card file was kept on individual couples as a central source of information and progress.

MATERIAL

Between January, 1952, and March, 1955, 185 couples were studied in this infertility clinic. No cases were included if there was less than 16 months of infertility. It should be emphasized that the type of patients seen in this clinic was different from the average uncomplicated, short-term infertility problem. A high percentage of our cases were referred and had been previously investigated elsewhere. In over half of the cases the previous diagnostic studies were incompletely or inadequately done.

METHODS

The female partner was advised that the first visit be arranged 6 to 12 days after the completion of her last menstrual period. The gynecologist obtained a complete history, with special emphasis given to the sterility problem. A complete physical and pelvic examination was done. Laboratory procedures included photoroentgenogram of the chest, protein-bound iodine studies, a complete urinalysis, a complete blood cell count, and serologic studies. A tubal insufflation was performed at the first visit. At the next examination, an endometrial biopsy was done one or two days prior to the anticipated menstrual period; also at this visit the basal temperature graph was interpreted.

The male partner was informed there should be three to five days of continence prior to his first examination. The urologist obtained a sterility history and performed a thorough physical examination, with emphasis on the genitalia. The laboratory investigation consisted of a urinalysis, examination of prostatic secretion, and a blood cell count. A protein-bound iodine study was done when indicated. The semen sample with a minimum continent period of three days preceding masturbation was examined by the urologist or a specially trained technician. Usually, two additional samples were requested before a definite opinion was rendered. The semen analysis consisted of pH determination, volume, liquefaction time, number of spermatozoa per milliliter, viability count by eosin-nigrosin stain, the number of abnormal forms, and the type of motility. In certain samples, duration of motility and survival after freezing were noted. Testicular biopsy was recommended on selected patients.

RESULTS OF FEMALE INVESTIGATION

Of the 185 women studied during two and one-half years, 156, or 84.3%, had never been pregnant. This corresponds closely with the experience of Turner and others.[1] A complete investigation was performed in 177 women. In eight instances, the investigation was not completed because of an immediate pregnancy or the discovery of a hopeless male factor, so that the couple did not wish further treatment.

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Read in the Symposium on Infertility Problems before the Section on Urology at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1955.

Dr. Eve Marberger evaluated the testicular biopsies made during the absence of Dr. Nelson.

1. Turner, V. H.; Davis, C. D.; Zanartu, J., and Hamblen, E. C.: Analysis of Clinical Data on 500 Childless Couples: Fertility Results, South. M. J. 44: 628-638 (July) 1951.

From the evidence of a biphasic basal body temperature graph or the biopsy evidence of a secretory endometrium, 90.7% of our female patients were ovulating. Obviously, this is indirect information based on the assumed presence of a corpus luteum proving ovulation has occurred. The question can logically be raised as to whether this is apparent only because of our incomplete knowledge concerning certain female diagnostic procedures and our inability to determine if

TABLE 1.—*Female Factors in Infertility*

Factor	No. of Patients
Amenorrhea	8
Endometriosis	8
Tubal obstruction	4
Fibromyoma	4
Previous ectopic pregnancy	4
Carcinoma in situ	3
Stein-Leventhal syndrome	2
Pelvic inflammatory disease	1
Psychosis	1
Ovarian failure	1
Total	36

normal healthy ova are always produced at ovulation. Only 11 patients had a proliferative endometrium and one a hyperplastic type. Of the 176 patients having one or more tubal insufflations with carbon dioxide, 97.7% had patent tubes with referred shoulder pain. There were only four patients with closed tubes, and five instances of tubal spasm were noted. Thus, one was impressed with how predominately normal the tubal findings were. Except for laboratory error or cases in which there had been previous iodine therapy, the protein-bound iodine levels were all within the range of normal, emphasizing that thyroid deficiency was not present.

There are still a number of physicians who feel that a freely movable retroverted uterus, a small uterus, cervical erosion, or a small external os are extremely important factors in infertility and require prompt attention. It is our feeling that a freely movable retroverted uterus is normal and is not a cause of infertility. A small external os or the presence of chronic cervicitis is seldom the cause of infertility. In 36 instances, or 19%, there were important clinical factors present that may have accounted for the female infertility. These are enumerated in table 1. Menstrual irregularities and endometriosis were the commonest factors, being present in 5.9 and 4.3% of the women. Other important complications giving rise to infertility were tubal obstructions, fibromyoma, previous ectopic pregnancy, and carcinoma in situ.

It is of interest that in only nine instances was surgery recommended to improve the female fertility. In two patients wedge resections of the ovaries were done because of a Stein-Leventhal syndrome. In three instances myomectomy was performed, and two patients had tubal plastic procedures. In one instance conservative operative therapy for endometriosis was carried out. Two of the eight patients operated upon have subsequently become pregnant.

RESULTS OF MALE INVESTIGATION

Of the men studied, 147 had a complete examination. In 2 patients the examination was incomplete, and 36 were not examined. In some instances, the wife conceived before the husband was examined, but it was surprising how often the latter was willing for his wife to be examined but was afraid to have his own fertility investigated for fear of damaging his ego.

Semen samples were obtained for examination from 152 men. The findings are tabulated in table 2. The incidence of absolute infertility in the male was 17.8% as compared to 11.6% in the female (those with closed tubes or permanent endocrine problems). Of 27 men with aspermia, 3 had no palpable vas deferens and a congenital absence was assumed. Two additional patients had surgically proved absence of the vas deferens. Of the 27 aspermic men, 5 consented to testicular biopsies and normal testes were found in 3, so it was assumed some obstructive factor was present. In the remaining two, testicular failure was demonstrated. The distribution of counts shows that about half the males had counts below 60 million. In general, it was found that the usual viability percentage throughout the series was lower (50%) than is observed by us in normal males (65% to 70%). Noteworthy was the observation that 10 men had consistent nonliquefaction of their semen. If the specimen after standing at room temperature for an hour in an open container did not fall in discrete drops from a medicine dropper, it was classified as nonliquefied. Only 2 of the 10 men with nonliquefaction had spermatozoal counts below 40 million per milliliter, and the nonliquefying aspect of the other 8 represented the only detected variation from normal. In each instance, liquefaction of the sample was accomplished with alpha-amylase, as described by Bunge and Sherman.[2] At the time this report was prepared no pregnancies had occurred with amylase-liquefied semen applied in a cervical cap.

One patient who had controlled diabetes had retrograde ejaculation into the bladder. On two separate occasions, in spite of preejaculatory and postejaculatory

TABLE 2.—*Results of Semen Analysis in Infertility**

Count/Ml., Millions	No.
No sperm	27
Up to 5	19
5 to 20	17
20 to 60	22
60 or over	67
Not done	32
Total	185

* Nonliquefaction was observed in 10 cases.

irrigations of the bladder with balanced salt solution, only dead sperm in abundant numbers were recovered. Drug therapy directed toward the internal sphincter of the bladder is now being tried.

On the basis of the low counts, testicular biopsies were recommended in many cases but were often refused. In 35 instances, biopsies were obtained, and the microscopic findings are shown in table 3. Although

2. Bunge, R. G., and Sherman, J. K.: Liquefaction of Human Semen by Alpha-Amylase, Fertil. & Steril. 5: 353-356 (July-Aug.) 1954.

several defects are usually observed in one testis, the major one is listed. In this series fibrosis and sloughing were seen most often. In only five males were the testes considered normal. The table shows which cases were selected for testosterone rebound therapy with some promise of success. This therapy should be predicated on histological findings and not used indiscriminately. Seventeen patients were treated, and 10 manifested rebound phenomena, with four pregnancies occurring in this period. In one case, the spermatozoal count rose and then fell to zero. The patient was given a second course of testosterone, and no rebound was detected during the ensuing one and one-half years.

TABLE 3.—*Results of Testis Biopsies in Infertile Males*

		Testosterone Treated		
		No.	Rebound	Pregnancy
Fibrosis	13	10	4	2
Fibrosis and sloughing	9	5	4	1
Spermatocytic arrest	4	1	1	0
Sclerosis	2	1	1	1
Normal	5	..	..	..
Totals	33	17	10	4 *

* One other pregnancy occurred after testosterone therapy. There was no testis biopsy.

PREGNANCIES

During the two and one-half years of the study, there were a total of 58 pregnancies achieved in the 185 couples studied (31.3%). This compares favorably with the results reported by Turner and co-workers,[1] King,[3] Frank,[4] and Johnson.[5] Of these 58 pregnancies, 45 occurred in the 156 couples with primary sterility and 13 pregnancies were reported in the 29 couples with secondary infertility.

The factors or procedures preceding the pregnancy are of considerable interest and are seen in table 4. In 16 cases female therapy was considered effective. Three of the five patients receiving estrogen therapy had been amenorrheic for over a year, and the therapy no doubt resulted in successful ovulation. In the two other patients, a small dose of estrogen was administered in the first half of the cycle to stimulate pituitary function. Of the 10 patients becoming pregnant following tubal insufflation or hysterosalpingography, 8 did so the following month. This is suggestive that the procedure was of therapeutic value. One patient became pregnant following wedge resection of the ovaries. In 13 women happenstance procedures such as a pelvic examination, endometrial biopsy, adoption, or the decision to discontinue sterility therapy really played little part in the pregnancy and the real factor was simply waiting or the psychological benefit.

It is difficult to assess the value of any particular form of therapy or even to be convinced that subsequent conceptions were in fact therapeutic successes and were not in part due to chance and time. Thus, in the female patients "therapy" was considered a factor in 50%, but time and chance seemed equally important.

The results of therapy in the male have been rather disappointing, but in nine instances pregnancy was achieved through treatment of the male. In five instances, the husband had been on testosterone rebound therapy and a pregnancy occurred within 5 to 12 months after completion of therapy. In two cases, we were unable to check the spermatozoal counts after the wives became pregnant. In 29 male patients having a low count the husband's semen was placed in a cervical cap at the time of ovulation, and in four patients a pregnancy occurred.

Therapeutic donor insemination was attempted in 34 patients, with a pregnancy being achieved in 20, or 58.8%, of the cases. In the 20 cases with conception, fresh semen was used in 11 and frozen semen in 9. The technique and results with frozen semen have been previously reported by Bunge and his co-workers.[6] The 26 patients receiving frozen donor semen were inseminated three times per cycle, and the nine conceptions occurred during the first or second cycle. None occurred later, even though some patients were inseminated in as many as seven cycles. Due to the fact that only 34.6% of the patients conceived with frozen donor semen, a change to fresh semen was made Nov. 1, 1954. With fresh semen, two attempts were made during each month with a cervical cap. Eleven pregnancies occurred in 20 patients, or 55%. Eight patients who did not become pregnant with frozen semen conceived with fresh semen. However, in some of these patients, conception did not occur until the third or fourth cycle. Two comparable series, using fresh and frozen semen in the cervical cap, would be needed to make any comparison of their relative value.

TABLE 4.—*"Therapeutic" Procedures Preceding Pregnancies in Infertility*

Female Factors	No. of Cases
Rubin's test	9
Hysterosalpingography	1
Estrogen therapy	5
Ovarian wedge resection	1
Total	16
Endometrial biopsy	3
Pelvic examination	3
Adoptions	4
Discontinued "therapy"	3
Total	13
Male Factors	
Cervical cap with husband's semen	4
Testosterone rebound	5
Total	9

Many authors have reported in the infertile female an increased number of abortions, ectopic pregnancies, and other prenatal complications. Of the 58 patients who became pregnant, 7, or 12%, aborted. Five of the seven abortions occurred prior to the eighth week, and all were confirmed by biological or histological determinations. This has convinced us that many of the so-called delayed periods reported by patients are often early abortions. Thirty-five of the patients delivered normal, healthy full-term infants; one child had defects present due to histoplasmosis. The only obstetric complica-

3. King, E. L., and Herring, J. S.: Sterility Studies in Private Practice, Am. J. Obst. & Gynec. **58**: 258-266 (Aug.) 1949.

4. Frank, R.: A Clinical Study of 240 Infertile Couples, Am. J. Obst. & Gynec. **60**: 645-654 (Sept.) 1950.

5. Johnson, W. O., and Marshall, J. B.: Pregnancy Following Sterility, South. M. J. **43**: 531-536 (June) 1950.

6. Bunge, R. G.; Keettel, W. C., and Sherman, J. K.: Clinical Use of Frozen Semen: Report of 4 Cases, Fertil. & Steril. **5**: 520-529 (Nov.-Dec.) 1954.

tion encountered was one case of placenta previa. Sixteen patients had not delivered at the time of writing. Thus, in our experience, the incidence of obstetric complications has not been increased.

COMMENT

The combined approach to the infertility problem has proved of value to the patient and to the interested physician. In this way a more complete and detailed examination is possible and new and different ideas can be evaluated. We have not used the group approach in interviewing or discussing therapy with the couple, but it is worthy of consideration.

In our study, we were impressed with the number of men with poor quality semen. If one uses the criterion of 60 million sperm per milliliter as being the lower limit of normal, then 56% of the men were subnormal in fertility. If one considers 20 million per milliliter as representing the lower limit of fertility, then 41.1% of the men were infertile. We were also surprised at the high percentage of women with patent tubes, normal basal temperature graphs, and secretory endometriums. In fact, there were relatively few women presenting true infertility by these criteria. Thus, in most of our discussions, we were forced to explain that, as far as we could tell, the female was normal but that perhaps her husband was responsible since he had a low or low-normal count.

In the field of infertility, so many diverse factors are involved that a sense of perspective is of prime importance. If one becomes particularly interested in any single factor, it is natural to exaggerate its importance. It is most difficult to evaluate results when a particular factor is corrected. It is so easy to be convinced that thyroid therapy, irradiation of the ovaries, treatment of a cervical factor, endocrine therapy, or psychotherapy may be of great importance in the successful treatment of infertility. We have found it most difficult to assess the value of any particular form of treatment, or even to be convinced that subsequent conceptions are therapeutic successes and not due at least in part to the effects of chance and time.

However, it is necessary to have a planned outline of treatment for the relatively infertile couple, as the realization that something is being done about their problem is of real importance to them. While the results of successful treatment of male infertility have not been encouraging, we feel the selected use of a cervical cap, testosterone rebound, and amylase may be of value.

SUMMARY

In 185 infertile couples studied during two and one-half years by a group of individuals interested in infertility problems, the higher incidence of male infertility as compared to female infertility is of interest. Fifty-eight, or 31.3%, of the women became pregnant. Twenty patients conceived through therapeutic donor insemination and 38 patients through treatment of the male or female.

MEDICAL OTOLARYNGOLOGY

Francis W. Davison, M.D., Danville, Pa.

Dr. J. M. Brown,[1] in his Chairman's address before the Section on Laryngology, Otology and Rhinology in 1947, made the following statement: "Otolaryngology in the future will become a specialty not only of surgical, but also of medical practice." Time has confirmed Dr. Brown's prediction.

In an effort to learn what occupies the otolaryngologist's time, I examined tht data for 1,000 consecutive new patients seen by me in 1954. Analysis showed that, if minor operations were excluded, only 20% of the 1,000 patients needed surgery. The other 80% needed good differential diagnosis, advice concerning their living habits, reassurance, minor psychotherapy, or drug therapy. This suggests that the otolaryngologist should be willing and able to assume the role of physician as well as surgeon for those patients whose symptoms send them to him. As medical and radiation therapy improve there will be still less need for surgery; this is real progress.

CHANGES IN OTOLARYNGOLOGY

Otolaryngology is a changed and greatly improved specialty, and this change is due largely to use of antimicrobic drugs and to better recognition and treatment of allergic conditions and autonomic dysfunction. As Dr. Brown said, the otolaryngologist must be an excellent allergist, immunologist, and practitioner of psychosomatic medicine.

• Deaths from the complications of otolaryngological infections declined sharply after the advent of sulfonamides and antibiotics. The practice of the otolaryngologist has changed accordingly, and most patients now need good differential diagnosis, instruction in hygiene, psychotherapy, and medication rather than surgery.

The frequency of mastoidectomies has diminished, but recent experience with ear infections shows that myringotomy has sometimes been neglected. Many patients with chronically discharging ears need surgical treatment, including radical mastoidectomy.

A patient with vertigo, tinnitus, or impaired hearing should have complete auditory and vestibular tests. Patients needing fenestration are referred to men especially skilled in this type of work, and urgent cases of respiratory obstruction can be handled best by specialists with requisite experience and equipment. The complaints of many patients prove to have a psychosomatic basis. Cancerophobia is frequent, but tumors are not infrequent. Patients who need radical cancer surgery should be referred to men who do this frequently.

From the Department of Otolaryngology and Broncho-Esophagology, the Geisinger Memorial Hospital and Foss Clinic.

Chairman's address, read before the Section on Laryngology, Otology and Rhinology at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1955.

1. Brown, J. M.: The Future of Otolaryngology, J. A. M. A. 135: 471 (Oct. 25) 1947.

Table 1 shows the mortality statistics for one 300-bed hospital. These statistics are typical of hospitals all over the country. It is notable that there were no deaths during the years 1951 through 1954. Reduction in morbidity and reduction in the number of operations necessary for drainage of pus have paralleled the decrease in deaths due to the complications of otolaryngological infections. From the data presented it seems obvious that penicillin by intramuscular injection is superior to the sulfonamides. It remains to be seen whether the "mycins" can, in a large series of cases, be as effective as penicillin by intramuscular injection in the treatment of serious infections due to penicillin-sensitive germs. In vitro tests to determine the sensitivity of the infecting organism can be helpful, but they are not a substitute for clinical judgment. Now, more than ever, the otolaryngologist must know bacteriology as well as the advantages and limitations of the available antimicrobic agents. As the result of promiscuous use of antibiotics, the number of organisms resistant to one or more of the "mycins" as well as the number of penicillin-resistant organisms is increasing. Therapeutic response does not always parallel the in vitro sensitivity test. This is because sensitivity tests as ordinarily used measure only the bacteriostatic and not the bactericidal action of the drug and because there is considerable variation in the amount of absorption of any antibiotic taken by mouth. Experience has shown that even intelligent use of antibiotics is not the answer to the problem of the patient with frequently recurring infections. We are just beginning to learn about hypogammaglobulinemia. A knowledge of the principles of immunology should be part of the equipment of every otolaryngologist. One of the more recent articles on this subject is "The Plasma Cell Theory of Antibody Formation," by Harry P. Schenck.[2] A textbook I frequently use is "Immunity, Hypersensitivity, and Serology," by Sidney Raffel.[3]

TABLE 1.—*Deaths from Complications of Otolaryngological Infections from 1932 to 1954 Inclusive*

Presulfonamide Period		Sulfonamide Period		Penicillin Period	
Yr.	Deaths	Yr.	Deaths	Yr.	Deaths
1932	6	1939	3	1945	1
1933	7	1940	3	1946	0
1934	8	1941	4	1947	3
1935	4	1942	0	1948	1
1936	7	1943	0	1949	0
1937	1	1944	1	1950	3
1938	8			1951-54	0
Total	41 in 7 yr., or about 6 per yr.	Total	11 in 6 yr., or about 2 per yr.	Total	8 in 10 yr., or less than 1 per yr.

TEAMWORK

Dr. Frederick Hill,[4] in his 1954 presidential address to the American Otological Society, made a plea for teamwork, by which he meant consultation with the internist, endocrinologist, pediatrician, psychiatrist, or neurological surgeon. I agree with this point of view but hasten to add that the 1,000 patients under discussion came to an otolaryngologist or were sent by their family physicians because they had symptoms in the anatomic areas ordinarily treated—or perhaps I should say examined—by an otolaryngologist. It seems logical that the general practitioner is competent to determine whether the symptoms are due to local disease or are local expressions of defects such as endocrine imbalance or disturbance of the autonomic nervous system, or are due to some type of allergy or faulty nutrition. The family physician must have a fair idea of the probable type of disturbance before he can decide which consultant to call.

It has been suggested that the general practitioner is competent to diagnose and treat the nonsurgical phases of otolaryngology. My experience does not support this statement. Of the 1,000 patients, 54% were referred because the conscientious practitioner realized that he needed help. The other 46% came for advice because their symptoms had not been relieved or their worries allayed by the one, two, or three general practitioners whom they had previously consulted. Anxiety tension states created by cancerphobia can be relieved by a skillful examination coupled with a convincing explanation of the mechanism of production of symptoms. Skillful examination requires the delicate sense of touch and highly developed monocular vision possessed by the otolaryngologist as the result of constant daily practice. Being conscious of our own limitations, we in turn frequently ask help from other departments. After the necessary diagnostic measures are carried out, the patient is sent back to the family physician.

The philosophy that has guided me was well expressed by Gordon Harkness[5] in his presidential address to the American Laryngological Association in 1954. He said: "1. The keystone of the practice of medicine is what is best for the patient. 2. The only justification for the existence of any special field of medicine is better care for the patient. 3. The prerogatives of a doctor of medicine are wide, but with them goes a solemn responsibility not to abuse them. Knowledge of some of the subdivisions of a special field of medicine may not be part of the equipment of every man basically well-trained in the fundamentals of his specialty." This philosophy has led me to refer patients requiring fenestration to men who are particularly skilled in this type of work.

Some type of allergy was a factor in production of symptoms in 22% of the 1,000 patients, and I do not classify autonomic dysfunction as an allergy. I think it is sensible for the otolaryngologist to be well grounded in the fundamentals of allergy and to make his own allergy studies. The majority of well-trained dermatologists do this. I agree with Dr. Hill's plea for teamwork in the management of every patient's problems, but I do not think it should be necessary for a rhinologist to refer 22% of his patients to an allergist. A properly trained otolaryngologist is in the best position to determine whether a patient's nasal symptoms are due to structural abnormality, infection, food or inhalant sensitivity, bacterial allergy, autonomic dysfunction, or to two or more of these factors, which are not mutually exclusive.

2. Schenck, H. P.: The Plasma Cell Theory of Antibody Formation: Its Importance in Interpretation of Physiology of Lymphoid Structures of Waldeyer's Ring, Ann. Otol. Rhin. & Laryng. **64**: 109 (March) 1955.

3. Raffel, S.: Immunity: Hypersensitivity, Serology, New York, Appleton-Century-Crofts, Inc., 1953.

4. Hill, F. T.: President's Address, American Otological Society, Ann. Otol. Rhin. & Laryng. **63**: 370 (June) 1954.

5. Harkness, G. F.: President's Address, Tr. Am. Laryng. A. **75**: 14, 1954.

Patients having head or face pain due to autonomic dysfunction gravitate to the office of the otolaryngologist because sinus disease is suspected. The otolaryngological literature of the last 10 years contains many important papers dealing with the subject of autonomic dysfunction. My understanding of this subject has been considerably improved by reading the contributions of Williams [6] and Hilger.[7]

EAR INFECTIONS

Ear infections still require the care of an otolaryngologist. Table 2 shows what has been accomplished. Mastoidectomy was necessary for many of these patients as they were referred to us late in the course of their disease, sometimes with complications indicating the necessity of immediate surgical treatment. Simple mastoidectomy has been necessary only six times in the last four years. None of these six patients had the benefit of myringotomy, and, if penicillin was used, it was given by mouth or in inadequate dose according to our standards. Judging from this experience, acute surgical mastoiditis can and should be completely eliminated by early myringotomy plus early administration of one of the antibiotics, preferably penicillin by intramuscular injection. In my experience,[8] failure to use myringotomy is responsible for the greatly increased number of patients with conduction deafness due to middle ear effusion.

TABLE 2.—*Decreasing Incidence of "Simple" Mastoid Operations at the Geisinger Hospital*

Yr.	Period	Cases of Acute Otitis Media and Mastoiditis, No.	"Simple" Mastoid Operations, No.	Percentage Requiring Mastoidectomy
1937	Presulfonamide	202	119	58.9
1943	Sulfonamide	282	74	26.2
1946	Small dose penicillin	247	10	4.0
1949	Large dose penicillin	189	5	2.7
1950	(1-3 million units daily)	158	9	5.7
1951	(1-3 million units daily)	109	1	0.9
1952	(1-3 million units daily)	110	3	2.7
1953	Larger dose penicillin	122	0	0
1954	(5-10 million units daily)	65	2	3.0

During the past 18 months, 123 patients with chronically discharging middle ears were examined in our department. Of these 123 patients, 42% needed surgical treatment, 36 needed radical mastoidectomy, and 17 had modified radical mastoidectomies. Proper choice of treatment for such patients requires the judgment of an experienced otolaryngologist and not the haphazard use of ear drops. Rehabilitation of the patient handicapped by hearing impairment is a problem requiring teamwork. Certainly no patient should acquire a hearing aid unless he has previously had an adequate medical history and careful examination by an otolaryngologist to determine whether the hearing defect can be lessened by medical or surgical therapy. Dr. Frederick Hill [4] sums up the problem in the following words: "Few otologists pretend to any but the most superficial knowledge of acoustics; and I would doubt more than a speaking acquaintance on the part of the audiologist with clinical otology. Consequently the importance of cooperation is obvious, not alone in research, but in the development of programs of conservation and rehabilitation."

To return to the 1,000 patients and a consideration of the ear symptoms, 31 patients had vestibular disturbance and 77 had some type of perceptive deafness. This makes a total of 108 patients, or 10.8% of the 1,000, who had some type of disorder of the inner ear. H. L. Williams' monograph [9] entitled "Ménière's Disease" is one of the best available guides to the understanding of these disorders. Great progress has been made during the last 10 years in the diagnosis and treatment of disorders of the inner ear. Most of this work has been done by otolaryngologists, and their papers appear in our specialty journals. Complete hearing and vestibular tests and a knowledge of their interpretation are necessary in the diagnosis of the symptoms of the patient suffering with deafness, tinnitus, or vertigo. The patient will receive better care from the man who is familiar with the papers of Hilger,[7] H. L. Williams,[6] the Fowlers, Sr. and Jr.,[10] and of Hoople.[11]

RESPIRATORY TRACT OBSTRUCTIONS

The diagnosis and treatment of respiratory tract obstructions present urgent problems that can best be solved by the man who is experienced in the use of direct laryngoscopy, bronchoscopy, and tracheotomy. The lifesaving measures necessary for treatment of acute laryngotracheobronchitis in children were described by the Jacksons [12] in 1936. Subsequent improvement in treatment methods have been made chiefly by other otolaryngologists, notably Thomas Galloway.[13] His small monograph entitled "The Treatment of Respiratory Emergencies Including Bulbar Poliomyelitis" is a masterpiece and should be read by all physicians who deal with problems of this type. Galloway was the first to demonstrate conclusively the value of tracheotomy in the treatment of bulbar poliomyelitis. Widespread use of the methods devised and taught by him have been responsible for the saving of hundreds of lives.

There are additional reasons why endoscopy is a logical part of the practice of otolaryngology. It seems obvious that the man who uses a head light or a head mirror all day long over one eye will have developed his monocular vision so that he should be a better bronchoscopist than the man who uses monocular vision for the performance of a bronchoscopy only three or four times a week. Another reason is the frequent coexistence of chronic infection in both the upper and lower respiratory tracts of the same individual. I am reasonably cer-

6. Williams, H. L.: A Concept of Allergy as Autonomic Dysfunction Suggested as an Improved Working Hypothesis, Tr. Am. Acad. Ophth. **55**: 123 (Nov.-Dec.) 1950; A Phylogenetic Concept of Allergy, Proc. Staff Meet., Mayo Clinic **24**: 516 (Sept. 28) 1949.

7. Hilger, J. A.: Vasomotor Labyrinthine Ischemia, Ann. Otol. Rhin. & Laryng. **59**: 1102 (Dec.) 1950.

8. Davison, F. W.: Otitis Media—Then and Now, Laryngoscope **65**: 142 (March) 1955.

9. Williams, H. L.: Ménière's Disease, Springfield, Ill., Charles C Thomas, Publisher, 1952.

10. Fowler, E. P., and Fowler, E. P., Jr.: Somatopsychic and Psychosomatic Factors in Tinnitus, Deafness and Vertigo, Ann. Otol. Rhin. & Laryng. **64**: 29 (March) 1955.

11. Hoople, G. D.: Practical Aspects of Labyrinthine Tests, Laryngoscope **59**: 12 (Jan.) 1949; The Evolution of Modern Office Audiometry, Ann. Otol. Rhin. & Laryng. **64**: 79 (March) 1955.

12. Jackson, C., and Jackson, C. L.: Acute Laryngotracheobronchitis: Living Pathologic Conditions Seen in Acute Respiratory Diseases, J. A. M. A. **107**: 929 (Sept. 19) 1936.

13. Galloway, T. C.: The Treatment of Respiratory Emergencies Including Bulbar Poliomyelitis, Springfield, Ill., Charles C Thomas, Publisher, 1953.

tain that I have better knowledge of how to treat the patient if I examine his nose and sinuses and make the bronchoscopic examination and the bronchograms when indicated.

MALIGNANCY AND PSYCHOSOMATIC DISEASE

Only 18 (1.8%) of the 1,000 patients had some type of malignant neoplasm, and 8 of these were in the esophagus, trachea, or bronchi. Two of the 18 had glomus jugularis tumors and were treated by roentgen therapy. Only 4 of the 18 cases were suitable for surgical therapy, and in only one case was a radical neck dissection needed. Patients needing radical cancer surgery should be referred to men who do it frequently.

A large number of patients with psychosomatic complaints come of their own volition or are sent to the office of an otolaryngologist because the family physician was not able to rule out organic disease to his or the patient's satisfaction. Of the 1,000 patients I examined, 26 had vascular (tension) headache; 45 had no disease of the ear, nose, and throat; 36 were suffering from anxiety tension state; 20 had cancerphobia; 47 had carotid pain, and 25 had cricopharyngeal spasm (globus). This makes a total of 199, or almost 20% of the 1,000. Such patients are no doubt regarded as nuisances by otolaryngologists interested solely in surgery; but, if we keep firmly in mind the idea that service to patients is our first responsibility, we must take the complaints of these people seriously. Mental suffering is often worse than physical suffering. Careful study of the book "The Nose" by Holmes, Goodell, Wolf, and Wolff [14] furnishes considerable insight into the management of these patients having psychosomatic symptoms. The article entitled "Carotid Pain" by Hilger [15] is another important reference.

KEEPING ABREAST

In order to keep abreast of developments outside the field of otolaryngology, I read THE JOURNAL of the American Medical Association. By scanning the table of contents on the front cover, one can quickly select the articles dealing with problems encountered in daily practice. In addition I find the Medical Literature Abstracts section of THE JOURNAL an important source of information.

Answers to an inquiry sent to otolaryngologists all over the country show that there is a great shortage of young men equipped to deal with the medical as well as surgical phases of otolaryngology. Better patient care is afforded by those otolaryngologists who are willing and able to treat both phases. As Dean Lierle [16] said at the 1955 American Academy of Ophthalmology and Otolaryngology teacher's section, the three year period of training advised by the American Board of Otolaryngology is basic and is designed for the general practice of otolaryngology. Patients are grateful for this type of service. I find it stimulating and rewarding.

14. Holmes, T. H.; Goodell, H.; Wolf, S., and Wolff, H. G.: The Nose: An Experimental Study of Reactions Within the Nose in Human Subjects During Varying Life Experiences, Springfield, Ill., Charles C Thomas, Publisher, 1950.

15. Hilger, J. A.: Carotid Pain, Laryngoscope **59**: 829 (Aug.) 1949.

16. Lierle, D. M.: Residency Training from the Viewpoint of the American Board of Otolaryngology, Tr. Am. Acad. Ophth. **59**: 106 (Jan.-Feb.) 1955.

CONTROL OF POTENCY AND THE DOSAGE OF DIPHTHERIA AND TETANUS TOXOIDS

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• The effectiveness of immunization to diphtheria, tetanus, and pertussis was studied in a group of infants between 2 and 6 months of age. Two dosage levels were tried. The titers for diphtheria and tetanus antitoxin and for pertussis agglutinin were determined a month after the injections and again at the end of a year. With but one exception, the larger dose resulted in the higher titer. The feasibility and advisability of immunizing infants starting between the second and sixth months was demonstrated. The alum-adsorbed toxoids gave better results than the fluid preparations. Assays in the guinea pig afford some indication of the effectiveness of toxoids in man. Since the size of the dose was found to be so important, the search for more accurate methods of assay is justified.

Most countries require manufacturers to control the immunizing efficacy of diphtheria and tetanus toxoids by minimum requirement tests. These tests generally consist of inoculating 10 or more guinea pigs with a prescribed dose of the prophylactic and after a suitable period either (*a*) challenging them with 10 or more lethal doses of the toxin concerned or (*b*) bleeding them, separating the serums and titrating them for specific antitoxin. In the first type of test, at least 80% of the animals must survive. In the second, the serums either pooled or individually (this varies in different countries) must contain antitoxin equal to or greater than an arbitrarily set amount.

Such tests have served, and will continue to serve, a useful purpose. It has been our experience, however, that both diphtheria and tetanus toxoids, prepared in the same manner but by different manufacturers, can vary widely in potency,[1] even though they have passed minimum requirement tests, and it has been apparent for some time that more precise assay procedures than these

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The immunizing agents used in these studies were specially prepared by the Connaught Medical Research Laboratories of the University of Toronto under the direction of Dr. P. J. Moloney.

Miss Frances Connell and Mr. E. J. Hamilton gave technical assistance in this study.

are necessary if we are to have more effective control of potency of these products. A proper assay should include a comparison with a known stable standard, and the test should be so designed that the degree of reliability of the results may be calculated from the data in the test itself. Such tests, unfortunately, are expensive and have been used only sparingly to date, since there has been no good evidence establishing that antigenicity as determined in the guinea pig is an accurate index of its potency for man. The present report describes two studies started one year apart specifically designed to obtain information on this point.

PROCEDURE

Infants of the Creche de Misericordia, Montreal, Canada, were used for both these studies. All were born in the institute of unmarried mothers. They were cared for in the institute until they were either adopted or sent to other adoption centers. In either event, the child was lost to our study after transfer from the Creche. All children had the same environment, and the care and feeding was the same for each child. Under the circumstances, they made a particularly suitable group for the proposed study. Immunization was started between the second and sixth month of life. The age of the 239 children observed in this study at the time immunization was started was 2 months in 34 children (14%), 3 months in 48 (20%), 4 months in 81 (34%), 5 months in 54 (23%), and 6 months in 22 (9%).

The procedure followed for immunization was three injections spaced one month apart. For each preparation, half of the infants received a dose of 0.5 ml. at each injection and the others 1.0 ml. A sample of blood, approximately 5 ml., was taken immediately prior to the first injection and again one month after the third injection. Further blood samples were taken one year after the third injection from a number of infants in study 1, but this was not possible for any in study 2 due to the infants' being sent to other adoption centers at a much earlier age than previously. The serums were tested individually for diphtheria antitoxin, tetanus antitoxin, and pertussis agglutinins. In assessing the results, the children with measurable antibodies in their preimmunization serums were not considered separately, since they were evenly distributed in the study. Including them gives a more accurate picture of what happens in practice.

Triple antigen, i. e., diphtheria and tetanus toxoids combined with pertussis vaccine, were used for both studies. The composition of the different lots is shown in table 1. Two preparations, lots 5-1 and 7-1, were used in study 1; and three, lots 10-1, 11-1, and 12-1, were used in study 2. All preparations contained the same number of organisms, 30 by 10^9 killed, phase 1 Hemophilus pertussis per milliliter. The two fluid products contained 50 Lf. diphtheria toxoid and 20 Lf. tetanus toxoid per milliliter. Two of the adsorbed preparations (purified toxoid) that were precipitated by aluminum phosphate, lots 5-1 and 10-1, had 20 Lf. of diphtheria and tetanus toxoid per milliliter, and the remaining purified toxoid precipitated by aluminum phosphate, lot 11-1, had 10 Lf. diphtheria toxoid and 5 Lf. tetanus toxoid per milliliter. The diphtheria and tetanus toxoids in each preparation were assayed in guinea pigs by methods described elsewhere [2] against Canadian standards and the results interpreted in terms of immunizing units—the international unit [3] in the case of tetanus toxoid, and the German unit (Schutzeinheit or SE) for diphtheria toxoid. At the time of writing, no international unit had been established for the latter. The results of the guinea pig assays were compared with the results obtained in infants. Attention should be paid to the relationship, or rather the lack of relationship, between the Lf. and the immunizing unit. The Lf. (flocculation unit) measures the ability of a toxoid to combine with standard flocculating antitoxin. It serves as a means for quantitatively measuring the yield of toxoid. It is particularly useful for measuring the amount of toxoid recovered during purification and for making up the final product. Unfortunately, the potency per Lf. varies with every type of toxoid and even with different batches of the same type of toxoid. For this reason it has limited value as an indicator of potency and cannot ordinarily be used for that purpose.

RESULTS

Preimmunization Serums.—Of the serums taken before immunization, 98 (41%) of 237 tested for diphtheria antitoxin had at least 0.002 units per milliliter, 5 (2%) of 235 tested for tetanus antitoxin had at least 0.001 units, and 9 (4%) of 238 tested had demonstrable pertussis agglutinins.

TABLE 1.—*Composition of Immunizing Preparations Used*

Lot No. and Preparation	Contents/Ml. Diphtheria Toxoid Lf.	Tetanus Toxoid Lf.	Killed Phase 1 Hemophilus pertussis Organisms $\times 10^9$	Aluminum Phosphate, Mg.
Study 1				
7-1 Fluid	50	20	30	0
5-1 PTAP *	20	20	30	6.0
Study 2				
12-1 Fluid	50	20	30	0
11-1 PTAP	10	5	30	2.5
10-1 PTAP	20	20	30	5.0

* Purified toxoid, aluminum-phosphate precipitated.

Postimmunization Serums.—The results of the antibody titrations on the serums taken after immunization are shown in tables 2 to 7. The following information is given in each table: the lot number and components of the different prophylactics, the dosage employed, the number of immunizing units administered, the titers obtained, and finally the average titer for each group. Following are some of the observations of our study.

Diphtheria Toxoid: The diphtheria antitoxin titers obtained in study 1 both for one month and one year after immunization are shown in table 2. It will be noted that in each group the individual antitoxin levels were generally higher and also that the average titer was higher as

1. Greenberg, L.: The Relative Immunizing Efficiency of Diphtheria Toxoid Preparations, Bull. World Health Organ. **12**: 751, 1955; The Relative Immunizing Efficiency of Tetanus Toxoid Preparations, ibid. **12**: 761, 1955.

2. Greenberg, L.; Morrell, C. A., and Gibbard, J.: The Biological Assay of Tetanus-Toxoid. J. Immunol. **46**: 333, 1943. Greenberg, L., and Robin, M.: The Biological Assay of Diphtherial Toxoid, ibid. **59**: 221, 1948.

3. World Health Organization: Expert Committee on Biological Standardization: Fifth Report, World Health Organization Technical Report Series 56, Geneva, Switzerland, World Health Organization, 1952, pp. 4-5.

the number of immunizing units administered was increased. One month after immunization, the children receiving three 0.5 ml. doses of the fluid toxoid, or a total of 15 immunizing units, had an average titer of 0.442 units of diphtheria antitoxin; those receiving three 1.0 ml. doses, or a total of 30 immunizing units, had an average titer of 0.501. One year later, their average titers were 0.325 units and 1.528 units of diphtheria antitoxin respectively.

For purified adsorbed toxoid lot 5-1, one month after immunization, the children receiving three 0.5 ml. doses of toxoid, or a total of 33 immunizing units, had an average titer of 1.168 units of diphtheria antitoxin, and those inoculated with three 1.0 ml. doses, 66 units, had an average titer of 1.409. One year later, their average titers for diphtheria antitoxin were 6.644 and 11.638 respectively. Similarly, in study 2, with one exception, the groups receiving the higher number of immunizing units also generally exhibited better antitoxin titers and higher average titers. This is shown in table 3. The single exception was the group receiving three 0.5 ml. doses (29 immunizing units) of fluid toxoid, lot 12-1, which had an average titer of 0.573 units of diphtheria antitoxin, compared with the infants receiving 58 units of the same lot and 62 units of lot 11-1, who had average titers of only 0.340 and 0.446 respectively. The other groups followed the pattern obtained in study 1.

Tetanus Toxoid: The tetanus antitoxin titers obtained in study 1, for the serums taken both one month and one year after immunization, are shown in table 4. The trend noted previously in the response to diphtheria toxoid, wherein the groups receiving the greater number of immunizing units also had higher group titers and higher group averages, was also evident here. In study 1, the average antitoxin titer one month after immunization was 0.150 antitoxin units for the group receiving 109 immunizing units of fluid toxoid, 0.305 units for the group receiving 218 immunizing units, and, for those receiving purified toxoid precipitated by aluminum phosphate, 1.071 for those receiving 437 immunizing units and 1.215 for those receiving 874 immunizing units. The one year results, also listed in table 4, show average tetanus antitoxin titers of 0.360, 1.493, 3.656, and 6.062 units respectively. The results for study 2 are shown in table 5. Unfortunately, our guinea pig assay for the tetanus toxoid fraction of lot 12-1 was unsatisfactory, and, since there was not enough material to carry out a repeat assay, we were unable to establish its potency in terms of units. Here too, as noted earlier with this lot of fluid toxoid, the average tetanus antitoxin response was greater with the lower dose (0.483 units as compared with 0.324). For the adsorbed toxoids, the children who received 126 immunizing units had an average titer of 0.477 antitoxin units, those receiving

TABLE 2.—*Diphtheria Antitoxin Titers in Children, Study One*

Toxoid, Lot No. and Composition	Dose, Ml.	Toxoid Units* Per Dose	Toxoid Units* Total	No. of Children	Antitoxin Units † 0	0.004	0.008	0.016	0.032	0.064	0.128	0.256	0.512	1.024	2.048	4.096	8.192	16.4	32.8	65.6	Av. Titer‡
1 Mo. After Immunization																					
7-1 (fluid)																					
50 Lf. diphtheria	3 × 0.5	5	15	24	..	..	1	3	2	4	2	5	3	3	..	1	..	..	..	..	0.442
20 Lf. tetanus																					
30 × 10^9 Hemophilus pertussis	3 × 1.0	10	30	28	..	..	..	2	1	6	2	4	8	4	..	1	..	..	..	..	0.501
5-1 (PTAP) §																					
50 Lf. diphtheria	3 × 0.5	11	33	34	..	..	..	..	1	2	1	6	8	9	4	2	1	..	..	..	1.168
20 Lf. tetanus																					
30 × 10^9 H. pertussis	3 × 1.0	22	66	35	..	..	..	..	1	..	1	4	6	14	5	3	1	..	..	..	1.409
1 Yr. After Immunization																					
7-1 (fluid)																					
50 Lf. diphtheria	3 × 0.5	5	15	7	1	..	2	1	..	1	1	..	..	..	1	..	..	..	..	..	0.325
20 Lf. tetanus																					
30 × 10^9 H. pertussis	3 × 1.0	10	30	11	2	1	2	1	..	..	1	1	..	..	..	2	1	..	..	..	1.528
5-1 (PTAP)																					
20 Lf. diphtheria	3 × 0.5	11	33	18	1	4	2	2	4	..	..	..	1	..	..	1	..	1	1	1	6.644
20 Lf. tetanus																					
30 × 10^9 H. pertussis	3 × 1.0	22	66	15	..	..	1	3	1	2	1	..	..	..	1	..	3	1	..	2	11.638

* Immunizing units.
† Actual titer greater than the amount specified at the top of the column but less than the amount in the next column.
‡ Arithmetic mean.
§ Purified toxoid, aluminum-phosphate precipitated.

TABLE 3.—*Diphtheria Antitoxin Titers in Children, Study Two, One Month After Immunization*

Toxoid, Lot No. and Composition	Dose, Ml.	Toxoid Units Per Dose	Toxoid Units Total	No. of Children	Antitoxin Units 0	0.008	0.016	0.032	0.064	0.128	0.256	0.512	1.024	2.048	4.096	Av. Titer
12-1 (fluid)																
50 Lf. diphtheria	3 × 0.5	9.7	29	19	1	2	1	1	1	4	2	3	..	4	..	0.573
20 Lf. tetanus																
30 × 10^9 Hemophilus pertussis	3 × 1.0	19	58	20	..	..	1	2	3	5	5	1	2	1	..	0.340
11-1 (PTAP) *																
10 Lf. diphtheria	3 × 0.5	20.7	62	20	..	1	1	..	5	3	2	3	4	1	..	0.446
5 Lf. tetanus																
30 × 10^9 H. pertussis	3 × 1.0	41.4	124	23	..	..	..	..	2	2	8	1	5	2	3	1.063
10-1 (PTAP)																
20 Lf. diphtheria	3 × 0.5	45.6	137	15	..	..	..	..	1	..	..	3	8	1	2	1.335
20 Lf. tetanus																
30 × 10^9 H. pertussis	3 × 1.0	91.3	274	19	..	..	..	..	2	1	1	1	4	5	5	1.886

* Purified toxoid, aluminum-phosphate precipitated.

252 immunizing units had 1.102 antitoxin units, those receiving 294 immunizing units had an average titer of 1.464 units, and those receiving 588 immunizing units an average of 2.129 antitoxin units.

Pertussis Vaccine: The responses to the different lots of pertussis vaccine are shown in tables 6 and 7. The unitage for the different preparations was not determined for reasons discussed later, but each lot had the same number of killed, phase 1 H. pertussis organisms. It will be noted that, in general, the agglutinin titers obtained with the adsorbed preparations were higher than those for the fluid.

Surveys [1] carried out at the Laboratory of Hygiene have shown wide differences in the potencies of preparations in use today. Assays were completed on diphtheria toxoids received from 20 laboratories in 11 countries and tetanus toxoids from 16 manufacturers in 10 countries. It was found that some lots of diphtheria toxoid were 189 times more potent than others, and even greater variations were observed in the tetanus toxoids. Furthermore, routine assays at the Laboratory of Hygiene have shown greater than fiftyfold differences in the potency of diphtheria and tetanus toxoids on the Canadian market (Canadian and United States manufacture),

TABLE 4.—*Tetanus Antitoxin Titers in Children, Study One*

Toxoid, Lot No. and Composition	Dose, Ml.	Toxoid Units: Per Dose	Toxoid Units: Total	No. of Children	Antitoxin Units: 0.008	0.016	0.032	0.064	0.128	0.256	0.512	1.024	2.048	4.096	8.192	16.4	32.8	Av. Titer
1 Mo. After Immunization																		
7-1 (fluid)																		
50 Lf. diphtheria	3 × 0.5	36.4	109	24	..	1	2	5	7	9	..	..	..	..	..	..	..	0.150
20 Lf. tetanus																		
30 × 10^9 Hemophilus pertussis	3 × 1.0	72.8	218	28	..	..	3	2	7	7	7	2	..	..	..	..	..	0.305
5-1 (PTAP) *																		
20 Lf. diphtheria	3 × 0.5	145.7	437	34	..	..	..	1	..	6	8	12	5	2	..	..	..	1.071
20 Lf. tetanus																		
30 × 10^9 H. pertussis	3 × 1.0	291.4	874	35	..	..	1	..	..	2	8	15	7	2	..	..	..	1.215
1 Yr. After Immunization																		
7-1 (fluid)																		
50 Lf. diphtheria	3 × 0.5	36.4	109	6	..	3	2	..	..	..	..	..	1	..	..	..	..	0.360
20 Lf. tetanus																		
30 × 10^9 H. pertussis	3 × 1.0	72.8	218	9	2	1	1	1	..	..	..	1	2	..	1	..	..	1.493
5-1 (PTAP)																		
20 Lf. diphtheria	3 × 0.5	145.7	437	17	2	2	3	4	2	..	..	..	..	1	1	1	1	3.656
20 Lf. tetanus																		
30 × 10^9 H. pertussis	33 × 1.0	291.4	874	13	..	..	1	2	2	..	1	..	2	..	3	1	1	6.062

* Purified toxoid, aluminum-phosphate precipitated.

TABLE 5.—*Tetanus Antitoxin Titers in Children, Study Two, One Month After Immunization*

Toxoid, Lot No. and Composition	Dose, Ml.	Toxoid Units: Per Dose	Toxoid Units: Total	No. of Children	Antitoxin Units: 0.032	0.064	0.128	0.256	0.512	1.024	2.048	4.096	8.192	Av. Titer
12-1 (fluid)														
50 Lf. diphtheria	3 × 0.5	?	?	19	1	1	3	6	6	..	2	..	..	0.483
20 Lf. tetanus														
30 × 10^9 Hemophilus pertussis	3 × 1.0	?	?	17	..	..	3	8	6	..	..	..	..	0.324
11-1 (PTAP) *														
10 Lf. diphtheria	3 × 0.5	42	126	20	..	1	6	4	7	..	2	..	..	0.477
5 Lf. tetanus														
30 × 10^9 H. pertussis	3 × 1.0	84	252	23	..	..	2	4	5	5	6	1	..	1.102
10-1 (PTAP)														
20 Lf. diphtheria	3 × 0.5	98	294	16	..	..	1	1	3	5	4	2	..	1.464
20 Lf. tetanus														
30 × 10^9 H. pertussis	3 × 1.0	196	588	19	..	..	..	..	3	4	9	2	1	2.129

* Purified toxoid, aluminum-phosphate precipitated.

COMMENT

The most effective immunization against diphtheria and tetanus (or in fact any disease) cannot be practiced unless suitable methods of estimating the immunizing efficiency of the prophylactic concerned are available and this defined in terms of standard immunizing units. The difficulties encountered in achieving this goal have created a tendency to ignore it, and most control laboratories depend almost entirely on minimum requirement tests for controlling the efficacy of their products. The latter tests have done much toward improving the quality of marketed products, but their value has definite limitations, and, although their use is widespread, there is little doubt that market preparations from various laboratories or that different lots from a laboratory vary widely in potency, albeit meeting minimum requirements, even though all of these products are controlled by identical minimum requirement tests.

It is evident from the above that more precise methods of control are necessary if we are to insure that only highly effective products are distributed. As mentioned previously, all products should be tested against a known stable standard, and the test itself should be so designed that the degree of reliability of results may be calculated from the data obtained in the test itself. The recent introduction of an international standard for diphtheria toxoid,[3] and a standard and international unit for tetanus toxoid,[3] should be of value in this regard. Unfortunately, the present international standard for diphtheria toxoid (plain) has its limitations.[4] Its immunization curve in

4. (*a*) Prigge, R.: Standardization of Diphtheria and Tetanus Toxoids, Bull. World Health Organ. **9**: 843, 1953. (*b*) Greenberg, L.: International Standardization of Diphtheria Toxoids, ibid. **9**: 829, 1953.

the guinea pig is so much flatter than that of most market toxoids that a high proportion of the assays are unsatisfactory. The adoption of an international standard for diphtheria toxoid, adsorbed, now being arranged by the World Health Organization Expert committee for biological standardization,[5] should do much to overcome the failings of the present standard, and, furthermore, the committee's intention to establish an international unit equal in potency to the German unit (the only country at present with an established unit) should prove of value.[5a] Attention should be paid to the term "unit" mentioned above. A toxoid unit is an antigenic unit and refers to the toxoid's ability to produce active immunity. This is quite distinct from and should not be confused with the "antitoxin" unit, which refers to the ability of an antiserum to neutralize toxin in vivo or in vitro.

Five preparations were used in the two studies reported here (table 1); two were fluid toxoids and three adsorbed. All were triple antigens containing diphtheria and tetanus toxoids combined with pertussis vaccine. The diphtheria and tetanus toxoid fractions were assayed in guinea pigs and the immunizing units determined for each. The results obtained in infants clearly show that the antigenicity as determined in the guinea pig is a direct indication of its value for man.

The response in infants to the diphtheria toxoid fraction was clearly related to the number of toxoid units given. In all but one instance the groups receiving the greater number of toxoid units exhibited higher antitoxin levels and had higher group averages. The correlation between the response to tetanus toxoid in infants and the toxoid unitage as determined in the guinea pig was equally striking. All the groups, with the exception of lot 12-1, for which it was not possible to complete the assay, showed the same picture noted above, i. e., the higher the toxoid unitage the better the group response.

No effort was made to determine the unitage of the pertussis vaccines, since it was considered that the potency tests presently used are not precise enough for this purpose.[6] Each preparation, however, had the same number of bacteria per milliliter—30 billion killed, phase 1 H. pertussis. It is interesting to note that the response, as measured by agglutinins, was higher in all cases in the alum preparations than it was for the fluid. The significance of pertussis agglutinins has not yet been established, but most of the available evidence [7] suggests that in infants there is a correlation between the agglutinin titer and immunity.

TABLE 6.—*Pertussis Agglutinin Titers, Study One*

Toxoid, Lot No. and Composition	Dose, Ml.	No. of Children	Agglutinin Titers * 0	2	4	8	16	32	64	128	256	512	1024	2048	Av. Titer
1 Mo. After Immunization															
7-1 (fluid)															
50 Lf. diphtheria	3 × 0.5	24	4	1	2	4	4	2	1	1	3	2	..	..	89.8
20 Lf. tetanus															
30 × 10⁹ Hemophilus pertussis	3 × 1.0	28	2	..	..	2	4	2	7	3	3	4	..	1	208.6
5-1 (PTAP) †															
20 Lf. diphtheria	3 × 0.5	34	1	..	1	..	4	4	9	4	5	5	..	1	210.9
10 Lf. tetanus															
30 × 10⁹ Hemophilus pertussis	3 × 1.0	35	1	1	..	..	..	1	8	4	6	7	6	1	410.6
1 Yr. After Immunization															
7-1 (fluid)															
50 Lf. diphtheria	3 × 0.5	7	2	2	..	1	..	..	1	1	..	..	..	..	29.1
20 Lf. tetanus															
30 × 10⁹ Hemophilus pertussis	3 × 1.0	11	3	1	..	..	1	..	4	..	..	1	1	..	164.5
5-1															
20 Lf. diphtheria	3 × 0.5	18	5	3	1	1	2	..	4	..	2	..	..	..	45.4
10 Lf. tetanus															
30 × 10⁹ Hemophilus pertussis	3 × 1.0	15	3	..	..	2	1	1	2	1	1	1	1	2	413.9

* Reciprocal of dilution of serum.
† Purified toxoid, aluminum-phosphate precipitated.

TABLE 7.—*Pertussis Agglutinin Titers, Study Two, One Month After Immunization*

Toxoid, Lot No. and Composition	Dose, Ml.	No. of Children	Agglutinin Titers * 0	4	8	16	32	64	128	256	512	1024	2048	4096	8192	16384	Av. Titer
12-1 (fluid)																	
50 Lf. diphtheria	3 × 0.5	19	8	2	1	2	4	..	1	..	..	1	..	..	..	..	69.9
20 Lf. tetanus																	
30 × 10⁹ Hemophilus pertussis	3 × 1.0	21	4	1	1	4	1	2	3	2	..	1	2	..	..	..	297.7
11-1 (PTAP) †																	
10 Lf. diphtheria	3 × 0.5	19	1	..	..	1	..	2	3	5	6	..	..	..	1	..	688.0
5 Lf. tetanus																	
30 × 10⁹ Hemophilus	3 × 1.0	23	..	1	..	..	2	1	1	3	4	7	1	2	..	1	1603
10-1 (PTAP)																	
20 Lf. diphtheria	3 × 0.5	16	..	..	..	..	2	3	3	2	3	2	..	1	..	..	552
20 Lf. tetanus																	
30 × 10⁹ Hemophilus	3 × 1.0	19	..	..	..	..	..	..	1	3	1	8	6	..	..	..	1152

* Reciprocal of dilution of serum.
† Purified toxoid, aluminum-phosphate precipitated.

5. (*a*) World Health Organization: Expert Committee on Biological Standardization: Eighth Report, World Health Organization Technical Report Series 96, Geneva, Switzerland, World Health Organization, 1955. (*b*) Footnote 3.

6. Morrell, C. A., and Greenberg, L.: The Practical Value of Sound Methods of Biological Assay, Fed. Proc. **13**: 808, 1954.

The conclusion that antigenicity of diphtheria and tetanus toxoids as measured in the guinea pig is a direct indication of their effectiveness for man is based on the examination of all of the results obtained in both studies. It is known that individuals vary widely in their antibody response even though they have received the same dosage and identical courses of immunization. One might, therefore, justifiably question the statistical significance of the differences in antitoxin titers obtained between two separate groups, i. e., between the subgroups receiving 15 and 30 units of diphtheria toxoid for lot 7-1 and those receiving 33 and 66 units for toxoid 5-1. However, the higher the toxoid unitage the better the antitoxin response, at least in infants. It is inconceivable that such uniform results were obtained by chance alone, and one must conclude therefore that the animal assay is an accurate guide of the effectiveness of these products in humans.

Factors Preventing Wider Use of Proper Assay Procedures.—Three factors have prevented the wider use of proper assay procedures in controlling the potency of these products. First, minimum requirement tests have done much to place effective products at our disposal, and the successes of the past have been such that there has been no obvious need for more elaborate methods of control that would add to the cost of immunization. Second, the exact relationship between antigenicity for the guinea pig and for man had never been satisfactorily established. Third, an assay can involve 100 or more guinea pigs, and, in the light of the first two reasons, the cost has been considered prohibitive. Further consideration should be given to this problem.

It is obvious that we cannot relax our immunization procedures against diphtheria for fear it might return with all its former severity. Furthermore, the occasional outbreak of diphtheria, even today, in populations believed well immunized is evidence of chinks in our immunization armor. There is, therefore, every reason for continued and increasingly vigorous programs of immunization. For this purpose, it is important that only the most effective toxoids be used. The procedures necessary for accurately standardizing toxoids are now available. We still have to determine the optimal effective dose for humans, since the use of too potent material is not only wasteful but overdosing may even depress antibody titer. Once this has been determined, however, consideration should be given to the establishment of accurate standardization procedures of at least diphtheria toxoid and the labeling of market preparations in terms of "toxoid" or "immunizing" units.

Superiority of Adsorbed Preparations.—These studies, moreover, reveal the superiority of the adsorbed preparations, for, while the fluid triple antigens used in these studies resulted in effective antibody titers for all three antigens, they were in no instance as effective as the adsorbed preparations. The Lf. concentration of the toxoids varied (table 1), and, when assessed on a comparable Lf. basis, the adsorbed products were found to be more effective for both the guinea pig and the child.

This raises the question of the use of fluid toxoids in public health immunization programs for infants. There is, on the part of public health officials in Canada at least, strong resistance to the use of alum products. This antipathy is based on the belief that (1) three doses of fluid toxoid are either as effective as three doses of alum or are at least all that is necessary, providing booster doses can be given at a later date, (2) alum toxoids are more likely to cause so-called sterile abscesses, and (3) during poliomyelitis epidemics paralysis of the injected limb is less likely to occur after immunization with fluid toxoid, which can be given subcutaneously, than with the alum, which is given intramuscularly. The validity of most of these beliefs is questionable.

The results in this report have shown that the fluid preparations, even when given in three doses, are not as effective as the alum. Furthermore, the purification of toxoid and the use of purer alum compounds have decreased the number of "sterile" abscesses to the point where they rarely, if ever, occur. Finally, alum toxoids, with the concentration of alum shown in table 1, can be administered subcutaneously; in fact, this route was used in the present study, and no difference in reactions was noted between the groups immunized with the adsorbed and with the fluid preparations. When one considers these results, and also the fact that in many instances infants do not return to health clinics for their second or third inoculations, a good argument for the wider use of alum products exists. These studies add further proof of the validity and desirability of starting immunizing during the first six months of age.

SUMMARY

Providing proper assay procedures are used, antigenicity of both diphtheria and tetanus toxoids as determined in the guinea pig is a direct indication of its effectiveness for the immunization of infants. It is possible to assay diphtheria and tetanus toxoids and evaluate their immunizing potency in terms of "immunizing units." The best possible results in immunization against diphtheria and tetanus cannot be obtained until accurate assay methods are used for determining the immunizing efficacy of the toxoids; these should be labeled in terms of immunizing units. These studies add further proof of the feasibility and advisability of immunizing infants starting between the second and sixth month of life.

7. Lapin, J. H.: Combined Immunizations, in Advances in Pediatrics, Levine, S. Z., editor, vol. 4, New York, Interscience Publishers, Inc., 1949.

Hormonal-Antibiotic Therapy.—Combined hormonal-antibiotic therapy, properly used, may result in lessened morbidity and mortality. Injudicious use of corticoids in such patients can produce precisely the opposite effect. The principles involved are as follows: 1. The vast majority of patients with infectious disease, as the result of the inflammatory reaction, the formation of specific immune bodies, endogenous adrenal cortex activity, and the proper use of antibiotics, make an uneventful recovery. 2. In a small group of patients, infection can result in fatality before the above agencies can be adequately mobilized. In such patients short-term, intensive corticoid therapy may result in rapid and profound diminution of systemic toxicity. Inhibition of the inflammatory reaction brought about by such therapy constitutes a potential hazard. This hazard can be adequately neutralized by the coadministration of properly indicated antibiotics and by discontinuance of corticoid therapy as rapidly as the patient's condition permits. It is essential that a precise program be followed.—L. W. Kinsell, M.D., and J. P. Jahn, M.D., Combined Hormonal-Antibiotic Therapy in Patients with Fulminating Infections, *A. M. A. Archives of Internal Medicine*, September, 1955.

PREVENTION OF RHEUMATIC FEVER BY TREATMENT OF PREVIOUS STREPTOCOCCIC INFECTIONS

EFFECT OF SULFADIAZINE

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• Patients receiving sulfadiazine for acute streptococcic pharyngitis were compared with patients receiving other therapy for the same condition. The sulfadiazine reduced the incidence of complications during the acute phase. After the first week, however, the incidence of suppurative complications was about the same in both groups. The streptococci were not eradicated. The subsequent incidence of recurrent pharyngitis in the sulfadiazine group was three times that in the contratest group, and the sulfadiazine did not prevent rheumatic fever.

For many years the sulfonamides were the only antibacterial drugs available for the therapy of acute streptococcic pharyngitis. Although such therapy was effective in reducing the duration of the illness and the incidence of the suppurative complications,[1] there is little information indicating whether or not it prevented the nonsuppurative complications, rheumatic fever and acute glomerulonephritis. In recent years, it has been demonstrated that the treatment of streptococcic infections with penicillin and other antibiotics will prevent the subsequent development of rheumatic fever.[2] Since many physicians continue to employ the sulfonamides in the treatment of streptococcic infections, it is important to establish whether such therapy will similarly prevent rheumatic fever. Therefore, in the present study, the treatment of acute streptococcic pharyngitis with sulfadiazine was evaluated with particular reference to the effect of such therapy on the attack rate of rheumatic fever.

METHODS

The clinical and laboratory methods employed have been described elsewhere.[3] The present study was part of a larger investigation [4] and included those airmen who were hospitalized with exudative pharyngitis or tonsillitis between April, 1953, and February, 1954. Excluded were all patients who gave a personal or family history of rheumatic fever, who had had a previous untoward reaction to penicillin or to sulfonamides, or who exhibited a suppurative complication at the time of the initial examination.

A total of 291 patients received 2 gm. of sulfadiazine initially, followed by 1 gm. every six hours for five days. Treatment was initiated on an average of 36 hours after the onset of symptoms, and for 92% of the patients therapy was started within 60 hours. A standard history and physical examination were recorded on admission and again 9, 13, 21, and 35 days after the onset of illness. Patients with manifestations suggestive of rheumatic fever were readmitted to the hospital for further observation. A culture specimen from the tonsils or oropharynx was obtained at the time of each examination.

The analysis was limited to 261 patients from whom group A streptococci were isolated at the time of admission to the hospital. Eighty-seven per cent of these patients harbored streptococci of types 3, 14, 19, or 30. Ninety-seven per cent of the patients were examined between 21 and 35 days after the onset of illness for evidence of rheumatic fever.

For purposes of comparison, a control group of 264 patients with exudative pharyngitis due to group A streptococci is included. These patients were selected and observed in the same manner as the patients treated with sulfadiazine, but they received only nonspecific therapy. Ninety-four per cent of the control patients were examined during convalescence. The two groups of patients appear to be comparable in that the historical and laboratory data obtained on admission were similar and the predominant serologic types of streptococci were the same. The control patients, however, were observed during the three-month period prior to the start of the present study.

RESULTS

In the dosages employed in this study, sulfadiazine did not eradicate the Streptococcus from the throat of patients with streptococcic exudative tonsillitis or pharyngitis (table 1). Nine days after the onset of symptoms, the infecting type of Streptococcus was isolated from more of the control patients than from those treated with sulfadiazine, which probably indicates continued suppression of the organism as a result of therapy. The carrier rates for the infecting type were equal in the two groups at 13, 21, and 35 days. Of those patients with bacteriological data available from all four examinations, the infecting type of Streptococcus was isolated at some time during the convalescent period from 88%

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1. Freis, E. D.: The Treatment of Tonsillitis with Small Doses of Sulfonamides, J. A. M. A. **126**: 93-94 (Sept. 9) 1944.
2. Houser, H. B., and Eckhardt, G. C.: Recent Developments in the Prevention of Rheumatic Fever, Ann. Int. Med. **37**: 1035-1043 (Nov.) 1952.
3. Wannamaker, L. W., and others: Prophylaxis of Acute Rheumatic Fever by Treatment of the Preceding Streptococcal Infection with Various Amounts of Depot Penicillin, Am. J. Med. **10**: 673-695 (June) 1951.
4. Catanzaro, F. J., and others: Symposium on Rheumatic Fever and Rheumatic Heart Disease: The Role of the Streptococcus in the Pathogenesis of Rheumatic Fever, Am. J. Med. **17**: 749-756 (Dec.) 1954.

of the group treated with sulfadiazine and from 93% of the control group. The acquisition rate for new types of streptococci was slightly less in the patients treated with sulfadiazine.

A recurrence of exudative pharyngitis or tonsillitis was observed in 21 of the treated patients (table 2). With one exception, the original infecting type of Streptococcus was again isolated at the time of recurrence of symptoms. The clinical relapse became manifest within one week after the completion of therapy in most instances. Therapy with one of the antibiotics was instituted in eight patients; four patients received no treatment during the relapse; and nine patients were given a second course of sulfadiazine. One of the latter patients subsequently developed rheumatic fever. In contrast, only seven patients in the control group developed a relapse, all of whom harbored the infecting type of Streptococcus at the time of the recurrence. One of these patients developed rheumatic fever following the second episode of exudative pharyngitis.

Suppurative complications, first recognized after at least 24 hours of therapy, were observed in 11 patients (4.2%) treated with sulfadiazine (table 2). In eight patients the complication developed after the completion of therapy, whereas three patients manifested the complication between the third and fifth days of treatment. In the control group, 17 patients (6.5%) developed suppurative complications. During the first week of illness, 12 control patients and 4 treated patients developed suppurative complications, indicating that such sequelae were reduced by sulfadiazine during this period. After the first week the incidence of suppurative complications was essentially equal in the two groups.

A diagnosis of rheumatic fever was established in 14 of 261 patients who were treated with sulfadiazine, an attack rate of 5.4% (table 3). The interval from the onset of symptoms of pharyngitis to the onset of rheumatic fever was between 1 and 35 days in all instances, and the infecting type of Streptococcus was again isolated from all 14 patients after the onset of the rheumatic episode. In addition, there were six patients who developed manifestations that are frequently associated with rheumatic fever, but the symptoms were mild and subsided spontaneously. In the control group, 11 patients subsequently developed rheumatic fever, an attack rate of 4.2%. The interval to the onset of rheumatic fever was between 1 and 37 days, and the infecting type of Streptococcus was isolated from nine patients after the onset of rheumatic fever.

TABLE 1.—*Effect of Treatment on the Persistence of Group A Streptococcus*

Type of Streptococcus Isolated at Convalescence as Compared with Admission Culture	Streptococcus Carriers, %							
	9 Days		13 Days		21 Days		35 Days	
	Sulfadiazine	Control	Sulfadiazine	Control	Sulfadiazine	Control	Sulfadiazine	Control
Same type	66	88	82	85	75	71	48	46
Different type	5	7	6	8	6	14	15	24
Group A Streptococcus not isolated	29	5	12	7	19	15	37	30

COMMENT

To evaluate an antibacterial agent in the treatment of an infectious disease, one criterion is the effectiveness of the drug in the elimination of the causative organism. As a general rule, with eradication of the organism the disease process will be terminated and complications will be prevented. Streptococcic infections differ from other infectious illnesses in that they are responsible for two nonsuppurative complications in which the infecting organism has not been directly related to the pathological lesions. These two diseases are rheumatic fever and acute glomerulonephritis. Recently, however, it has been shown that rheumatic fever develops after a streptococcic infection only if the organism persists in the oropharynx.[4] Therefore, it would appear that the effect of therapy on the morbidity and complications of streptococcic infections can also be related to its effect on the infecting organism.

The results of this study would indicate that the administration of sulfonamides during the acute phase of streptococcic pharyngitis will reduce the incidence of suppurative complications. That such a reduction is related to the effect of the drug on the infecting organism is shown by the fact that the complications were prevented only during the period of therapy, when the growth of the Streptococcus was suppressed. Following the cessation of therapy and with the regrowth of the organism, suppurative complications occurred at the same rate as in the control group of patients.

The therapy of acute streptococcic pharyngitis with sulfadiazine was attended by an incidence of recurrent pharyngitis that was three times the rate observed in nontreated patients. The relapse was apparently due to the original infecting type and in most instances required additional therapy. The most likely explanation is that sulfadiazine temporarily inhibited the growth of the Streptococcus and induced a remission in the manifesta-

TABLE 2.—*Recurrent Pharyngitis and Suppurative Complications Developing After at Least Twenty-Four Hours of Therapy*

	Interval to Complication *				Total	
	2-7 Days	8-14 Days	15-21 Days	22-28 Days	No.	%
Sulfadiazine						
Recurrent pharyngitis	0	18	2	1	21	8.0
Suppurative complications						
Peritonsillar cellulitis	2	2	1	0	5	1.9
Otitis media	1	3	0	1	5	1.9
Sinusitis	1	0	0	0	1	0.4
Control						
Recurrent pharyngitis	2	4	1	0	7	2.7
Suppurative complications						
Peritonsillar cellulitis	9	3	0	0	12	4.6
Otitis media	2	1	0	0	3	1.1
Sinusitis	1	1	0	0	2	0.8

* Interval is from onset of acute illness to onset of complication.

tions of the disease. The reduction in the number of organisms presumably diminished the stimulation of antibody formation [4] so that the patient did not develop immunity to the infecting Streptococcus. After therapy was completed, the organism again proliferated and a clinical relapse occurred.

Although acute pharyngitis or tonsillitis due to group A streptococci can be a prolonged and serious disease, particularly when suppurative complications supervene, the acute condition is seldom life-endangering or permanently disabling. For this reason, the primary concern in the treatment of such infections is the prevention of the nonsuppurative complications, rheumatic fever and acute glomerulonephritis. In the present study, the attack rate of rheumatic fever in the patients treated with sulfadiazine was slightly greater than in the control patients and was almost twice the usual incidence of 3% seen in untreated patients.[5] The obvious inability of such therapy to prevent rheumatic fever is apparently due to its ineffectiveness in the eradication of the Streptococcus. Recent investigations have indicated that persistence of the Streptococcus is essential for the development of rheumatic fever [4] and that therapy which prevents rheumatic fever also results in the elimination of the organism.[6] Since treatment with sulfadiazine does not significantly reduce the convalescent carrier rate, such therapy should not be expected to affect the attack rate of rheumatic fever.

Rheumatic fever can be prevented by the use of antibacterial agents for prophylaxis against infection by group A streptococci or for therapy of the acute streptococcic illness.[2] The daily administration of sulfonamides or penicillin will prevent infection by group A streptococci,[7] but the application of this prophylactic measure has been limited to special groups such as rheumatic subjects and military or institutional populations. Therefore, the only practical method available for the prevention of rheumatic fever in the general population is by therapy of the streptococcic infection itself. At the present time, it would appear that a single injection of benzathine penicillin G is the most effective means of preventing rheumatic fever in the patient with acute streptococcic pharyngitis.[8] Other forms of penicillin, chlortetracycline, tetracycline, erythromycin, or oxytetracycline, administered for at least 10 days, are also effective. Sulfonamides should not be employed in the treatment of streptococcic infections.

TABLE 3.—*Nonsuppurative Complications Occurring in 261 Patients with Streptococcic Pharyngitis Who Were Treated with Sulfadiazine*

Cases	Interval to Rheumatic Fever, Days	Joint Manifestations *						Carditis †	Fever ‡	Elevation of ESR §	Abdominal Pain
		P	R	T	S	Mult.	Mig.				
Definite Rheumatic Fever											
1	1	+	0	+	0	+	0	+	+	+	0
2	7	+	0	+	0	+	+	+	+	+	0
3	10	+	0	+	0	+	+	+	0	0	+
4	11	+	0	+	0	+	+	+	+	+	0
5	13	+	0	+	0	+	0	0	+	0	+
6	14	+	0	0	0	+	0	+	+	+	0
7	17	+	0	+	0	0	0	+	+	+	0
8	19	+	0	0	0	+	0	+	0	+	0
9	19	+	0	+	0	+	+	0	+	0	+
10	24	0	0	0	0	0	0	+	+	+	0
11	25	+	0	+	0	+	+	+	+	+	0
12	32	+	+	+	+	+	+	0	+	+	0
13	35	+	0	+	+	+	+	0	+	+	0
14	35	+	0	+	0	+	+	0	+	+	0
Possible Rheumatic Fever											
15	1	+	0	+	0	+	+	0	0	+	0
16	6	+	0	+	0	+	+	0	0	0	0
17	10	+	0	+	0	+	+	0	0	+	0
18	16	+	0	0	0	+	+	0	0	+	0
19	16	+	0	+	0	0	0	0	+	+	0
20	19	+	0	0	0	0	0	+	+	0	0

* P, pain; R, redness; T, tenderness; S, swelling; Mult., multiple; Mig., migratory.
† P-R interval of 0.22 second or greater, partial or complete auriculoventricular block, significant change in heart murmur, or pericardial friction rub.
‡ Temperature of 100.2 F (37.9 C) or greater.
§ Erythrocyte sedimentation rate 15 mm. or more in an hour by the Wintrobe method.

SUMMARY

Two hundred sixty-one patients with exudative pharyngitis due to group A streptococci were treated with sulfadiazine for five days. Sulfadiazine did not eradicate the Streptococcus from the respiratory tract and did not prevent rheumatic fever. Sulfonamides, therefore, should not be employed in the treatment of acute streptococcic pharyngitis. It should be emphasized that sulfonamides employed in prophylaxis against infection with group A streptococci have proved to be of great value in the prevention of such streptococcic infections and that the drug should continue to be utilized as a prophylactic measure.

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5. Rammelkamp, C. H., Jr.; Denny, F. W., and Wannamaker, L. W., in Rheumatic Fever, a Symposium Held at the University of Minnesota on Nov. 29-Dec. 1, 1951, Under the Sponsorship of the Minnesota Heart Association, Thomas, L., editor, Minneapolis, University of Minnesota Press, 1952, pp. 72-89.

6. Catanzaro, F. J.; Chamovitz, R.; Morris, A. J., and Rammelkamp, C. H., Jr.: Unpublished data.

7. Denny, F. W., in Streptococcal Infections, McCarty, M., editor, New York, Columbia University Press, 1954, pp. 176-196.

8. Chamovitz, R.; Catanzaro, F. J.; Stetson, C. A., and Rammelkamp, C. H., Jr.: Prevention of Rheumatic Fever by Treatment of Previous Streptococcal Infections: I. Evaluation of Benzathine Penicillin G, New England J. Med. **251**: 466-471 (Sept. 16) 1954.

CLINICAL NOTES

RAPID TEST FOR ADRENOCORTICAL INSUFFICIENCY

PRELIMINARY REPORT

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At the January, 1955, meeting of the New York Academy of Science on hydrocortisone, it was affirmed by Forsham and associates [1] that intravenously used hydrocortisone was useful in the treatment of operative and postoperative shock. In the ensuing discussion, as has been so often noted, it was stated that it would be desirable to assay the adrenal function of such patients before therapy was started; however, the precarious clinical state of the patients precludes any test that would delay the onset of therapy. Thus, it appeared that a test that would not delay specific corticoid therapy, that would be a satisfactory assay of adrenal status, and that could be completed in a few minutes would indeed be of great clinical value in evaluating which cases of operative and postoperative shock are due to adrenocortical hypofunction.

Such a rapid test of adrenal function might also be helpful in the diagnosis of adrenal insufficiency in patients with iatrogenic hypoadrenocorticism, an induced disease that is no longer rare. Bilateral adrenalectomy, with resultant adrenal cortical hypofunction (Addison's disease), is being performed for the treatment of severe hypertension,[2] for adrenal cortical hyperfunction (Cushing's syndrome),[3] and for cancer of the breast and prostate.[4] In addition, a still larger number of patients are developing adrenal atrophy as a result of the adrenocortical inhibition caused by the administration of cortisone, hydrocortisone, or corticotropin (ACTH). These patients may have inadequate adrenocortical reserve for months after the cessation of corticoid therapy.[5]

During the past two years, we have been able to corroborate the clinical impression of adrenocortical insufficiency in patients who were in medical shock within one hour after seeing them. The method consists of the simultaneous determination of the concentration of sodium in the serum and urine. The interpretation of the results depends upon the following physiological facts: 1. In the normal subject, hyponatremia, which follows salt deprivation or extrarenal salt loss, is associated with a marked renal tubular reabsorption of sodium, with a resultant minimal urinary salt excretion. 2. If the renal tubules are damaged (salt-losing nephritis) or if there is a deficiency of adrenal mineralocorticoids (Addison's disease), the renal tubules are unable to absorb sodium adequately; thus, there is a persistent urinary salt loss despite hyponatremia and decreased body-salt stores. Using these physiological facts, one may predict what the urinary and serum concentration of sodium in various states should be (table 1).

METHOD

A catheter is placed in the bladder if the patient is unable to void spontaneously, and a few cubic centimeters of urine are collected. Then 5 cc. of blood is withdrawn from a vein, the syringe is removed from the needle, and an intravenous drip of therapeutic fluid can be started at once. Thus, while the patient is receiving therapy, the serum and urinary concentrations of sodium are determined by a flame photometer. Since only 1 cc. of serum and 5 cc. of urine are needed for the accurate analysis of the sodium concentration by means of a flame photometer, adequate specimens can be obtained even if the patients are in shock and the veins are collapsed. If necessary, blood can be obtained from the femoral veins.

TABLE 1.—*Urinary and Serum Concentration*

Type of Patient	Serum Sodium	Urinary Sodium
Salt-poor control	Low	Very low
Salt-losing nephritis	Low	Moderate to high
Adrenal insufficiency	Low	Moderate to high

RESULTS

This report consists of the findings in eight patients who have had moderate to marked hyponatremia, dehydration, hypotension, and tachycardia. Thus they suffered from medical shock as a result of decreasing circulating blood volume secondary to sodium loss. Three patients had been on a severe salt-restricted diet as part of the therapy for cirrhosis in two and hypertensive cardiovascular disease in the other. Two patients had adrenocortical insufficiency; one had primary adrenal failure, and the other had hypopituitarism with secondary adrenal insufficiency. Of the final three patients, two were in the end stages of severe renal failure due to pyelonephritis and one was in the acute phase of anoxic tubular necrosis (lower nephron nephrosis). Table 2 reveals that the serum sodium concentration in all the subjects was considerably below the normal range of 137 to 142 mEq. per liter. It is quite significant that the urinary excretion of the three patients with normal renal and adrenal function was only 5, 8, and 13 mEq. per liter and that the urinary sodium concentration was considerably higher in the five patients with either renal tubular or adrenocortical insufficiency.

COMMENT

Although the basic physiological facts upon which the test is based are well known, they have rarely been applied to clinical medicine. Moore,[6] in an excellent discussion of the low sodium syndromes of surgery, has indeed stressed the importance of studying the urinary

From the Maimonides Hospital of Brooklyn and the Department of Medicine, State University of New York College of Medicine at New York City.

1. Rukes, J. M.; Orr, R. H.; Forsham, P. H., and Galante, M.: The Use of Intravenous Hydrocortisone in Major Surgery, Ann. New York Acad. Sc. **61**: 448 (May 27) 1955.

2. Green, D. M.; Nelson, J. N.; Dodds, G. A., and Smalley, R. E.: Bilateral Adrenalectomy in Malignant Hypertension and Diabetes, J. A. M. A. **144**: 439 (Oct. 7) 1950.

3. Sprague, R. G.; Kvale, W. F., and Priestley, J. T.: Management of Certain Hyperfunctioning Lesions of the Adrenal Cortex and Medulla, J. A. M. A. **151**: 629 (Feb. 21) 1953.

4. Huggins, C., and Scott, W. W.: Bilateral Adrenalectomy in Prostatic Cancer: Clinical Features and Urinary Excretion of 17-Ketosteroids and Estrogen, Ann. Surg. **122**: 1031 (Dec.) 1945.

5. Salassa, R. M.; Bennett, W. A.; Keating, F. R., Jr., and Sprague, R. G.: Postoperative Adrenal Cortical Insufficiency: Occurrence in Patients Previously Treated with Cortisone, J. A. M. A. **152**: 1509 (Aug. 15) 1953.

6. Moore, F. D.: The Low Sodium Syndromes of Surgery: An Outline for Practical Management, J. A. M. A. **154**: 379 (Jan. 30) 1954.

salt excretion as well as the serum sodium concentration. He pointed out that in the salt-deficient state, a high urinary salt concentration is indicative of renal tubular damage or adrenocortical insufficiency. However, despite this lucid presentation, these observations have been used infrequently to study adrenocortical function in the patient with either medical or surgical shock.

Moore and Ball [7] have demonstrated that there is an intensive adrenocortical activity in the postoperative state. This adrenocortical activity causes the renal tubules to absorb most of the salt from the glomerular filtrate, thus resulting in marked decrease of urinary sodium concentration. In both the postoperative shock state as well as in the hyponatremic medical shock state, the urinary salt excretion should be minimal unless there is either adrenocortical or renal tubular insufficiency. Desoxycorticosterone does not decrease the high urinary saline concentration due to salt-losing nephritis as it does in the adrenocortical-deficient state.[8] Thus, one can differentiate between these two causes of renal salt loss.

TABLE 2.—*Sodium Concentration in Serum and Urine of Eight Patients*

Disease	Serum Sodium, mEq./Liter	Urinary Sodium, mEq./Liter
Salt deprivation		
Cirrhosis	121-129	9-13
Cirrhosis	130	8
Hypertension	124	5
Adrenal insufficiency		
Adrenal cortical hypofunction	123-124	131-169
Hypopituitarism	121	163
Renal tubular insufficiency		
Pyelonephritis	121-130	74-94
Pyelonephritis	119	53-67
Acute renal tubular necrosis	134	147

With the availability of methods for determining serum concentrations of 17-hydroxycorticoids (cortisone and hydrocortisone acetate)[9] as well as the above-described test for quickly assaying mineralocorticoid function, the status of adrenocortical activity can now be rapidly determined. Although immediate therapy may be started before the results of these tests are available, in most cases, within one day, a definitive diagnosis may be made. Thus future therapy can be planned on a more rational basis.

SUMMARY

Hyponatremia associated with medical or surgical shock may be due to extrarenal salt loss or deprivation; this status is associated with a decreased urinary salt concentration. On the other hand, hyponatremia due to either renal tubular damage or adrenocortical insufficiency is associated with increased urinary saline concentration. A rapid, simple test will differentiate between these two groups of patients without delaying the initiation of therapy. Studies to extend this observation further and to use this method to predict the reserve status of adrenal function are in progress.

4802 10th Ave. (19).

7. Moore, F. D., and Ball, M. R.: Metabolic Response to Surgery, Monograph in American Lectures in Surgery, no. 132, Springfield, Ill., Charles C Thomas, Publisher, 1952.

8. Thorn, G. W.; Koepf, G. F., and Clinton, M., Jr.: Renal Failure Stimulating Adrenocortical Insufficiency, New England J. Med. **231**: 76 (July 20) 1944.

9. Eik-Nes, K.; Nelson, D. H., and Samuels, L. T.: Determination of 17,21-Hydroxycorticosteroids in Plasma, J. Clin. Endocrinol. **13**: 1280 (Oct.) 1953.

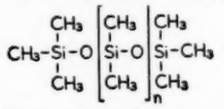
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

Monographs and supplemental statements on drugs that appear in this column have been authorized by the Council for publication and inclusion in New and Nonofficial Remedies. They are based upon the evaluation of available scientific data and reports of investigations.

H. D. KAUTZ, M.D., *Secretary.*

Dimethicone.—A silicone oil consisting of dimethylsiloxane polymers and technically designated as dimethylpolysiloxane of the D. C. 200 series of fluids. The structural formula of dimethicone may be represented as follows:



Actions and Uses.—Dimethicone, a silicone oil with skin-adherent and water-repellent properties, is useful for incorporation into ointment bases as a skin protective agent. Either greasy or relatively nongreasy preparations may be suitable, depending upon the conditions of exposure for which protection is desired. Greasy bases generally are better tolerated on skin that is excessively dry or that may be exposed to drying effects, but they may not be feasible in some industries. Relatively greaseless bases are subject to the disadvantage of easier removal and thus may provide less continuous protection. When applied to the skin in such vehicles, dimethicone imparts a coating effect that generally is resistant for a variable period of time to ordinary soap and water and to water-soluble irritants. Its resistance to nonsoap detergents and oil-miscible substances is less certain and there is some difference of opinion regarding its ability to repel organic solvents and different types of industrial oils. These differences appear to be influenced by the type of vehicle, although the comparative length of time for which protection is afforded by various preparations has not been determined. There is also lack of evidence to demonstrate that a given preparation of dimethicone offers better protection than use of the base alone. The addition of dimethicone, however, is regarded as an advance in the field of skin protective preparations.

Dimethicone is relatively inert and exerts no therapeutic action. It therefore is considered useful for topical application only as a prophylactic against exposure to dermal irritants and to ordinary cleansers and water when these are irritating or interfere with the healing of dermal lesions. Its use has been less successful in preventing dermal contact with household detergents and fuels than with soap and water. The effectiveness of dimethicone also is limited in preventing water or soap from aggravating lesions of chronic dermatoses, such as eczema. Except in chronic dermatoses aggravated by substances that can be repelled by dimethicone, it should be restricted generally to application on the normal skin. The agent may be irritating to the skin of infants and thus is of questionable utility for the prevention of am-

moniacal dermatitis (diaper rash). Because of its semiocclusive nature, dimethicone also may be harmful when applied to an acute dermatitis, or otherwise inflamed, traumatized, abraded, or excoriated skin. Likewise, it should not be applied over lesions that require free drainage, such as infected decubitus ulcers, fissures, fistulas, and sinuses. It can be used to prevent maceration and irritation of the skin surrounding such lesions as well as ileostomies and other operative stoma associated with irritating discharges; however, it is not considered helpful in controlling anogenital pruritus, which is seldom caused by associated discharges and may be aggravated by ointment preparations.

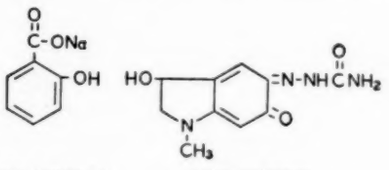
Dimethicone does not appear to sensitize the normal skin, but physicians should be alert to the possibility of sensitization from components of the ointment vehicle with which it is incorporated. As used in a base of white petrolatum, three or four surgical-type scrubbings may be required for its removal. Industrial workers should be warned against using solvents to hasten removal, as such agents also may give rise to occupational dermatoses. Dimethicone should not be used in the eyes because it produces a temporary smarting.

Dosage.—Dimethicone is applied to the skin in various types of ointment bases. A 30% concentration is used in white petrolatum; other concentrations may be better suited for other types of bases. The area to be protected should first be thoroughly cleansed with soap or a suitable substitute and water. The smallest amount necessary to cover the area should be applied uniformly and rubbed in thoroughly. Initially, application is made three to four times daily for one or two days, then one or two times daily depending upon the nature and frequency of exposure. With a greasy type base, any stickiness that remains after application can be minimized by wiping with a dry cloth or washing gently with soap and water, without removing the protective film. With relatively greaseless bases, care must be exercised to avoid removal during exposure, and more frequent daily applications may be required to provide protection.

Preparations for use as stated for the foregoing drug are marketed under the following name: Silicote.

Arnar-Stone Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of dimethicone.

Carbazochrome Salicylate.—Adrenochrome monosemicarbazone sodium salicylate complex.—The structural formulas of sodium salicylate and adrenochrome monosemicarbazone may be represented as follows:



Sodium Salicylate Adrenochrome Monosemicarbazone

Actions and Uses.—Carbazochrome salicylate is a derivative of adrenochrome, an oxidation product of epinephrine, proposed for systemic control of capillary bleeding characterized by increased capillary permeability. The drug does not affect blood pressure, cardiac rate or output, blood clotting mechanism, massive hemorrhage, or arterial bleeding. The use of the drug as a systemic hemostatic is based upon uncontrolled case reports of clinical observers who reported beneficial effects after oral or parenteral administration in controlling the bleeding associated with idiopathic purpura, retinal hemorrhage, familial telangiectasia, epistaxis, hemoptysis, and hematuria. Carbazochrome salicylate also is claimed to be of value in controlling postpartum hemorrhage and postoperative bleeding associated with tonsillectomy, adenoidectomy, surgery of the nasopharynx, prostate, bladder, chest, and teeth. The drug appears to be relatively nontoxic, and such untoward effects as might arise from repeated use are likely to result from sensitivity to the salicylate component.

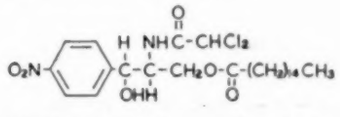
In the reports of clinical studies so far available there is a lack of adequately controlled clinical evidence to prove that cessation of capillary bleeding can be attributed to the action of this drug. Its clinical usefulness for this purpose is scientifically unestablished.

Dosage.—The drug has been administered orally or intramuscularly. The proposed oral dose for adults ranges from 1 to 5 mg. four times daily. The intramuscular dose, which may produce pain during injection, is 5 mg. every 2 to 4 hours. Dosage for children is reduced proportionately.

Preparations for use as stated for the foregoing drug are marketed under the following name: Adrenosem Salicylate.

S. E. Massengill Company cooperated by furnishing scientific data to aid in the evaluation of carbazochrome salicylate.

Chloramphenicol Palmitate.—D-(-)Threo-1-(*p*-nitrophenyl)-2-dichloroacetamido-1,3-propanediol 3-palmitate.—The structural formula of chloramphenicol palmitate may be represented as follows:



Actions and Uses.—Chloramphenicol palmitate represents the esterification of the antibiotic to a tasteless substance for the purpose of circumventing the bitter taste inherent in the parent drug. In the upper intestinal tract, the ester is hydrolyzed back to free chloramphenicol by the action of pancreatic and intestinal lipases. Its chemotherapeutic activity therefore is produced almost solely by release of active chloramphenicol, since the ester itself is practically devoid of antimicrobial action. Absorption of released chloramphenicol is somewhat slower than that of the free antibiotic, but blood levels persist for longer periods of time. The ester may be employed in the treatment of all infections for which the parent drug is indicated. Since chloramphenicol palmitate possesses the same inherent toxicity as the parent drug, the restrictions specified under chloramphenicol apply also to the palmitate; thus, adequate blood studies should be made when prolonged or intermittent administration is required. (See the monograph on chloramphenicol in New and Nonofficial Remedies.)

Dosage.—Chloramphenicol palmitate is given orally. Since the dosage is expressed in terms of the parent drug, it is the same as for orally given chloramphenicol.

Preparations for use as stated for the foregoing drug are marketed under the following name: Chloromycetin Palmitate.

Parke, Davis & Company cooperated by furnishing scientific data to aid in the evaluation of chloramphenicol palmitate.

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SOME HEALTH IMPLICATIONS OF THE WHITE HOUSE CONFERENCE ON EDUCATION

The most controversial feature of the recent White House conference was the question of federal aid for education. Interestingly enough, conference recommendations on this question were comparable with those of medicine in relation to medical education. Delegates, unanimously as far as could be judged, wanted no part of federal control of education. A strong majority reportedly favored federal aid for building construction and renovation. There was vigorous opposition to any federal aid for educational operations; however, federal aid was only one of several questions discussed. One of the others in particular had significant implications for the health of school-age children.

This was the issue of crowded school conditions. Delegates agreed that under present plans it is "virtually impossible" for most states to meet school building needs. This means too many children crowded into some schools, double sessions for others, too long bus rides for others, and the occupancy of unsafe outmoded buildings for still others. With these conditions come health problems, with which the physician is all too familiar. The accident hazard is increased, communicable disease control becomes more difficult, and personal health problems are multiplied. Regardless of stepped-up building programs, there can be no quick end to these troubles in many places; production of children has run too far ahead of construction of school buildings. In the interim, the difficulties must be dealt with realistically in the best interests of the children. This must be done at the local level, where the primary responsibility for education and health rightfully belong.

Formulation of programs that will best meet the needs of each individual community situation is legally the business of the board of education, or the school trustees. However, each citizen also has a responsibility to support the soundly conceived policies of these elected representatives. Physicians have a special obligation in this connection. Professionally they have the competency to give helpful advice and council on many of the issues involved. More important, they hold a position in the community that offers opportunity to provide constructive leadership in school affairs.

CONGRESS ON MEDICAL EDUCATION AND LICENSURE

During the program of the Congress on Medical Education and Licensure, scheduled February 11-14, 1956, at the Palmer House in Chicago, problems of general interest to members of the medical profession in private practice, to those in medical education, and to those responsible for medical licensure will be discussed.

In cosponsorship with the Advisory Board for Medical Specialties, this year the Council on Medical Education and Hospitals is devoting an entire day to a conference on graduate medical education. Current problems in this field will be reviewed. Special attention will be given to the organization and administration of a residency program, the means of effectively incorporating basic medical science into such programs, degree programs, investigations, and the psychiatric viewpoint in resident training. This rapidly growing area of medical education is deserving of close scrutiny, evaluation, and continued and varied experimental approaches. The tendency toward the application of rigid and inflexible patterns in graduate medical education should be meticulously avoided, and conferences of this type should prove of value in this while keeping the high standards sought by all concerned with this area of medical education.

The Council on Medical Education and Hospitals is also cosponsoring, with the Council on Medical Service, a program on problems related to clinical faculty appointments and the private practice of medicine. In view of the numerous evidences of difficulty, concern, and misunderstanding that have developed between medical schools and the medical profession in certain areas, it is believed that this area should be presented in the program for general discussion. Summaries will be given of information obtained through questionnaires submitted to medical schools and to medical societies in regard to their opinion on various facets of the situation. A summary of legal opinion dealing with the possibilities arising in connection with such programs will also be presented. The problem will then be interpreted as it concerns medical school administration and as it concerns the medical profession by representatives of these groups. Discussion of various programs now used in medical schools will aid institutions in determining those methods that function most effectively and to the best mutual advantage of the school and the profession at large.

The final half-day of the Council program will be devoted to the "search for better ways" in medical education. This will be initiated through a critical look at medical education, after which some new approaches and experimental programs will be briefly outlined. The portion of the Congress presented by the Federation of State Medical Boards of the United States will concern important problems of reciprocity and interstate endorsement, the final report of the committee on the essentials of a modern medical practice act, internship as related to medical licensure, relation of medical education to licensure, and foreign medical graduates. The Advisory Board for Medical Specialties will meet to discuss problems of mutual concern. Because of the wide interest in this Congress, hotel reservations should be made soon.

ORGANIZATION SECTION

THE JOURNAL INDEX

The index to volume 159 of THE JOURNAL appears in this issue. Those who wish extra copies of the index may receive them without charge on request to the Order Department, American Medical Association, 535 N. Dearborn St., Chicago 10, Ill.

MICHIGAN STATE SOCIETY HONORS LOS ANGELES COUNTY ASSOCIATION

The Los Angeles County Medical Association has been honored by the Michigan State Medical Society for pioneering in the medical television field with the show, "Medic." On behalf of the association, Dr. Ewing L. Turner, association president, accepted the Michigan plaque at ceremonies in the Los Angeles County Medical Association Headquarters from Mr. Hugh W. Brenneman, public relations counsel of the Michigan State Medical Society. The plaque cited the association for its sponsorship of and technical assistance to the highly successful television show and commended it for "outstanding service to both the American public and the medical profession."

Dr. Turner, in accepting the award, complimented the association's radio and television committee, headed by Dr. James F. Regan, chairman, for doing "a yeoman's job in working with the 'Medic' staff, putting in countless hours of tedious work to assure success of the program." Dr. Turner also had high praise for the staff of Medic Productions, Inc., complimenting the producer and other "Medic" staffers for "their genuine and sincere interest in the proper portrayal of medicine to the vast television viewing audience."

The following persons were among those present. From the Los Angeles County Medical Association: President Turner; Dr. J. Norman O'Neill, secretary-treasurer; Dr. James F. Regan, chairman, radio and television committee; Drs. Eugene F. Hoffman and Edward W. Rosenow Jr., councillors. From the A. M. A.: Dr. E. Vincent Askey, Vice-Speaker of the A. M. A. House of Delegates and Los Angeles County Medical Association past-president; and Mr. Leo E. Brown, Director of Public Relations. From the Michigan State Medical Society: Mr. Hugh W. Brenneman, director of public relations, and Mr. A. Dewitt Brewer, assistant public relations director. From Dow Chemical Co., cosponsors of "Medic": Mr. Arthur Smith Jr., director of public relations, and Mr. L. H. Woodman, assistant public relations director. From Medic Productions, Inc.: Mr. Frank LaTourette, producer, and Miss Gloria Votsis, director of public relations. From the Los Angeles County Medical Association staff: Mr. Jerry L. Pettis, public relations counsel; Mr. Bert Fitzgerald, business manager; Mr. K. C. Young, executive secretary; and Mr. Carl Dyster, managing editor of *The Bulletin*.

"Medic," which is seen Mondays at 9 p. m. EST on the NBC television network, is cosponsored commercially by the Dow Chemical Company and General Electric. Scientific and technical guidance to insure medical accuracy has been provided by the Los Angeles County Medical Association continuously since the show was created by Mr. James Moser and first telecast on Sept. 13, 1954.

The Michigan State Medical Society's plaque reads:

Whereas, the weekly television production entitled Medic presents a realistic and dignified portrayal of recent progress in medical knowledge and techniques, enlightening millions of Americans on the role of today's Doctor of Medicine in modern society, and

Whereas, Medic has cultivated public esteem for the medical profession as a whole, fostered the concept of private practice, gained favorable recognition of the philosophy of service held by the Doctor of Medicine, and widened appreciation for the discipline to which the ethical physician voluntarily complies, and

Left to right: E. Vincent Askey, M.D., Vice-Speaker, A. M. A. House of Delegates and past-president of Los Angeles County Medical Association; Frank LaTourette, producer of "Medic"; Hugh W. Brenneman, director of public relations of the Michigan society; Ewing L. Turner, M.D., Los Angeles County Medical Association president; and Arthur Smith Jr., director of public relations, Dow Chemical Co.

Whereas, production of Medic would have been impossible without the cooperation and guidance of the Los Angeles County Medical Association, Los Angeles, California, and the many hours of technical assistance which individual members of that Association contribute week by week; therefore be it

Resolved, That the Michigan State Medical Society warmly commends the Los Angeles County Medical Association for outstanding service to both the American Public and the Medical Profession through its co-sponsorship of Medic and sincerely expresses the deepest gratitude of their Michigan colleagues to every member of the Los Angeles Association who has given his time and talent toward the success of that production.

Robert H. Baker, M.D.
President

H. Fernald Foster, M.D.
Secretary

MEDICAL NEWS

CALIFORNIA

Annual Radiological Conference.—The eighth annual midwinter Radiological Conference, sponsored by the Los Angeles Radiological Society, will be held at the Biltmore Hotel, Los Angeles, Feb. 25-26. Out-of-state speakers will include Dr. R. McWhirter, Edinburgh, Scotland, Dr. Narno Dorbecker, Mexico City, Mexico, Dr. Philip J. Hodes, Philadelphia, and Dr. David G. Pugh, Rochester, Minn. General chairman of the conference is Dr. Robert B. Engle, St. Luke Hospital, Pasadena. Reservations may be made through the Conference Secretary, Dr. Norval F. Zimmerman, 3875 Wilshire Blvd., Los Angeles 5. A banquet ($7 per plate) preceded by cocktails will be held at the Biltmore on Saturday evening. The conference fee, $20, includes two round-table luncheon meetings. Courtesy cards for the conference are available to radiology residents and radiologists in military service, by advance registration.

Oto-Ophthalmologic Convention.—The Research Study Club of Los Angeles announces its 25th annual midwinter clinical convention in ophthalmology and otolaryngology, Jan. 16-27. Guest lecturers on otolaryngology (Jan. 16-20) include Dr. Benjamin H. Shuster, Philadelphia, Dr. French K. Hansel, St. Louis, Dr. Edmund P. Fowler Jr., New York, and Chauncey D. Leake, Ph.D., Columbus, Ohio. Guest lecturers on ophthalmology (Jan. 23-27) include Drs. F. Bruce Fralick and Harold F. Falls, Ann Arbor, Mich., and Dr. David O. Harrington, San Francisco. On Jan. 19, 7 p. m., the annual banquet of the Los Angeles Society of Ophthalmology and Otolaryngology will honor the guest lecturers of that week in the El Venado Room of the Elks Club. The American Laryngological, Rhinological, and Otological Society, western section, will hold its annual meeting in San Francisco between the two weeks of this convention, on Jan. 21. The fee for the entire two weeks, or any part of it, ($100) includes the cost of all luncheons. Checks should be made payable to Mid-Winter Clinical Convention and mailed to Dr. Norman Jesberg, Treasurer, 500 S. Lucas Ave., Los Angeles 17.

CONNECTICUT

Lecture on Gout.—The arthritis study unit, Yale University School of Medicine, New Haven, will present "Primary and Secondary Gout" by Dr. Alexander B. Gutman, director, department of medicine, Mount Sinai Hospital, New York City, Jan. 19, 3:30 p. m., in the Fitkin Amphitheater.

Panel on Peptic Ulcer.—The Hartford Medical Society will present Jan. 16 at 8:30 p. m. a panel on the peptic ulcer, with Dr. Benjamin V. White, Hartford, as moderator and Drs. Richard Warren, Boston, and Thomas E. Machella, Philadelphia, as guest speakers. All physicians are invited to attend.

Community Health Forums.—The first of three community health forums, sponsored by the Hartford County Medical Association in cooperation with the Hartford *Times*, is scheduled for the evening of Jan. 19 at the Horace Bushnell Memorial Hall in Hartford. Topics for the forums will be determined by a newspaper poll to ascertain the health subjects of greatest public interest. The forums, which will be open to the public free of charge, will comprise presentations by panels of physicians and question periods for audience participation.

Firemen's Grant for Leukemia Research.—The Tommy Memorial fund, which is sponsored by the firemen in New Britain, has given the Yale University School of Medicine, New Haven, its second grant ($6,000) for leukemia research. The first grant of $8,000, made in December, 1953, was turned over to Dr. Milton J. E. Senn, chairman, department of pediatrics, and to Dr. David H. Clement, associate clinical professor of pediatrics, who will also receive the new grant for their continuing study of new drugs in the treatment of leukemia. The study has been carried on chiefly in the pediatrics clinic of the Yale-New Haven Medical Center.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Society News.—DuPage County Medical Society in cooperation with the Chicago Heart Association will hold a dinner meeting Jan. 18, 6:30 p. m., at Memorial Hospital of DuPage County, 189 Avon, Elmhurst (TErrace 2-6800). At the scientific meeting, 8 p. m., "Rheumatic Carditis" will be presented by Dr. Oglesby Paul, associate clinical professor of medicine, University of Illinois College of Medicine, Chicago. All physicians are welcome.

Life Expectancy Rates.—According to the Metropolitan Life Insurance Company (1 Madison Ave., New York City), expectation of life at birth in Illinois at the midcentury was 66.0 years for white males and 71.6 years for white females. For the United States population as a whole, as reported by the National Office of Vital Statistics, Public Health Service, the comparable figures are 66.3 years for males and 72 years for females. The midcentury figures for Illinois mark a gain of 3.1 years for males and 4.1 years for females over those for 1940.

Chicago

Chandler Memorial Program.—The Chicago Orthopaedic Society presented the Fremont A. Chandler memorial program Jan. 13 at the Palmer House:

Nonsurgical Treatment of Bone and Joint Tuberculosis, Theodore A. Fox, Chicago.
Hoarseness and Painful Deglutition Due to Massive Cervical Exostoses, Charles V. Heck, Chicago.
Memorial Lecture, Alfred R. Shands Jr., Wilmington, Del.

Bacon Lecture.—The Charles Sumner Bacon Lecture for 1955-1956 will be delivered at the University of Illinois College of Medicine (1853 W. Polk St., room 221) Jan. 18-19 by Dr. Frederick H. Falls, professor emeritus, department of obstetrics and gynecology. At 1 p. m. Wednesday Dr. Falls will consider the anatomy and embryology of the uterus bicornis, and Thursday at 4 p. m., "Associated Obstetrical Complications."

Symposium on Duodenal Ulcer.—The metropolitan Chicago chapter of the American College of Surgeons offers a program, "The Medical and Surgical Management of Duodenal Ulcer," at the John B. Murphy Memorial Auditorium, 50 E. Erie St., at 8 p. m., Jan. 19. Dr. Walter C. Alvarez will be the moderator. The following physicians will speak and sponsor their residents on the following topics:

Karl A. Meyer, Resection Theory
Lester R. Dragstedt, Surgery and Vagotomy.
Warren W. Furey, X-Ray Aspect of Duodenal Ulcer.
Samuel H. Kraines, Role of Psychiatry in Duodenal Ulcer.
Clifford J. Barborka, Medical Management of Duodenal Ulcer.

The panel symposium will be followed by a question and answer period. Interns and residents are urged to attend.

Citterman Scholarship.—The first Solomon Citterman Scholarship was recently awarded to Zdenek Hruban, senior medical student. Mr. Hruban first began medical studies in Germany during World War II, was unable to complete them when Russia took over the East Zone of Germany, transferred to a medical school in Czechoslovakia, and again was interrupted by the establishment of the Communist Czech government in 1948. He came to the United States in 1951 and entered the University of Chicago Medical School. Income from the scholarship fund, established last January, will be awarded annually to medical students in need of financial assistance. Selection of the recipient of the scholarship is made by the university's scholarship committee on the basis of academic record and financial need.

Society News.—The Society of Medical History of Chicago will hold an open meeting at the Institute of Medicine (fourth floor, 86 E. Randolph St.) Jan. 18, 8 p. m. Dr. E. M. K. Geiling will

have as his topic "John Jacob Abel, Founder of American Pharmacology," and Dr. Leo M. Zimmerman "Iconography of Medical Interest in Painting and Sculpture."——The Medical Directors Club of Chicago was organized Nov. 3, 1955, at a meeting at the Drake Hotel. The following officers were chosen: Dr. Herbert R. Atherton, medical director, Swift and Company, president; Dr. Richard J. Bennett, United States Steel Company, vice-president; and Dr. Carl T. Olson, division medical director, Liberty Mutual Insurance Company, secretary-treasurer. The club will have monthly meetings. It will promote interchange of information and experience in the field of industrial medical administration; encourage better understanding between members of management and industrial medical administrators; and stimulate interest in, and better teaching of, industrial medical practice on the part of medical schools.

IOWA

Dr. Cooney to Speak on Atomic Energy.—Dr. James P. Cooney, deputy surgeon general, U. S. Army, will speak on some phase of atomic energy at the annual meeting of the Polk County Medical Society, Jan. 18, at the Des Moines Golf and Country Club.

KENTUCKY

Dr. Underwood Joins Public Health Service.—Dr. E. Bruce Underwood, Louisville, secretary-general manager of the Kentucky State Medical Association and state health commissioner, has resigned these posts and will leave on Feb. 1 for Washington, D. C., where he will be affiliated with the U. S. Public Health Service and work under the Hill-Burton program of federal aid for the building of hospitals.

MASSACHUSETTS

Personal.—Dr. Robert B. O'Connor, Boston, has been appointed medical director for the United States Steel Corporation to succeed Dr. J. Huber Wagner, Pittsburgh, who will serve as chairman of a United States Steel medical advisory committee on his retirement in January, after 35 years of service. Dr. O'Connor has been assistant professor of industrial medicine at Harvard School of Public Health, Boston.

Dr. Faulkner Honored.—Dr. James M. Faulkner, former dean of the Boston University School of Medicine, was honored recently when colleagues presented his portrait to the school. Dr. Faulkner, who served as head of the Boston University School of Medicine from 1948 to 1955, left the post to become medical director at Massachusetts Institute of Technology, simultaneously resuming his part-time teaching at Boston University as professor of clinical medicine. Dr. Paul Dudley White spoke briefly, recalling "Jim" Faulkner's student days at Harvard and at Massachusetts General Hospital. Dr. Chester S. Keefer, successor to Dean Faulkner as director of the school, accepted the portrait on behalf of the school.

MISSOURI

Hospital News.—The Jewish Hospital of St. Louis has been awarded $131,640 under the terms of the Hill-Burton Hospital Construction Act for a unit for diagnosis and treatment in adult psychiatric patients. The unit will be on the fifth floor of the Mark C. Steinberg Memorial Hospital, now under construction on the Parkview Place frontage of the Jewish Hospital medical center. The hospital has also received $600,000 from the Steinberg Charitable Trust and Mrs. Ellen S. Berkman and Mrs. Etta Steinberg, daughter and widow, respectively, of the late Mark C. Steinberg, to underwrite a new inpatient child psychiatric center at the hospital. A contribution of $18,702 has been received from Nat Koplar and Dr. and Mrs. Jacob G. Probstein of St. Louis and Sol Koplar of Chicago to furnish a hydrotherapy section. The rehabilitation division is part of the 7-million-dollar expansion program that will increase the capacity of the medical center from 298 beds and 42 bassinets to 475 beds and 50 bassinets. Construction should be completed about the end of 1956.

NEBRASKA

Society News.—At the 1955 annual meeting of the Omaha Mid-West Clinical Society, Dr. Maurice E. Grier was installed as president, and Dr. Charles F. Moon was elected president-elect. Dr. James J. O'Neil was reappointed director of clinics. The 1956 meeting will be held at the Fontenelle Hotel, Omaha, Oct. 29-Nov. 1.

Obstetric Conference.—The second annual winter obstetric conference of the University of Nebraska College of Medicine, Omaha, Jan. 19-20, will stress toxemia of pregnancy, including some of the technical aspects of electrolyte balance and the effects of aldosterone. Among the speakers will be Dr. J. Robert Willson, chairman, department of obstetrics and gynecology, Temple University School of Medicine, Philadelphia.

NEW YORK

Society News.—Newly elected officers of the New York Allergy Society include: Dr. Murray M. Albert, Brooklyn, president; Dr. Samuel J. Prigal, New York, president-elect; Dr. Leoni N. Claman, New York, vice-president; Dr. Aaron D. Spielman, New York, secretary; and Dr. Joseph H. Fries, Brooklyn, treasurer.

Joint Meeting.—The Medical Society of the County of Kings and the Academy of Medicine of Brooklyn will hear Jan. 17 in the MacNaughton Auditorium "Long-Term Experience in the Management of Patients with Diseases of the Heart" by Dr. Paul Dudley White, Boston. Dr. Louis Bauer, Hempstead, L. I., Past-President of the American Medical Association, will consider "The Present and Contemplated Program of United Medical Service (Blue Shield)."

Sanitary Code Amended.—The following amendment to the state sanitary code, effective July 1, 1959, was recently adopted by the state public health council: "Whenever milk or milk products are to be sold or offered for sale or delivered to consumers after pasteurization, all herds providing such milk shall be brucellosis-free in accordance with the applicable rules and regulations of the New York State Department of Agriculture and Markets or in accordance with the corresponding State agency having jurisdiction of animal health for the area in which the herd is located, which are accepted by the New York State Department of Agriculture and Markets as equivalent to the rules and regulations adopted by their Department."

New York City

University News.—Dr. Salvatore di Palma has been promoted to clinical professor in the department of obstetrics and gynecology of New York University College of Medicine. Dr. di Palma has served for 30 years in New York City's Bellevue Hospital Center, Harlem Hospital, and the New York City Cancer Hospital, where for 12 years he was director of the women's division.

Harvey Lecture.—Dr. Charles H. Rammelkamp, professor of medicine, Western Reserve University School of Medicine, Cleveland, and director, Streptococcal Disease Laboratory, Warren Air Force Base, Wyo., will deliver the fifth Harvey Lecture of the 1955-1956 series at the New York Academy of Medicine Jan. 19, 8:30 p. m., on "The Epidemiology of Streptococcal Infections."

Course on Cancer.—A course on cancer is being offered Jan. 23-Feb. 4 by the Post-Graduate Medical School, a unit of the New York University-Bellevue Medical Center. Entitled "The Basic Problems of Cancer Therapy," the full-time course is intended to give to the practicing surgeon comprehensive information on the fundamentals and the most recent developments in research, as well as diagnosis and treatment of the patient with cancer. The course will be under the direction of Dr. David Lyall, professor of clinical surgery. Among the topics to be covered are the application of radiation therapy and the evaluation of new radiation and chemotherapeutic treatments of cancer.

New Metropolitan Hospital.—A new 27-million-dollar hospital was recently completed as a replacement for the 80-year-old Metropolitan Hospital on Welfare Island. The new hospital

(97th to 99th streets, between First and Second avenues, Manhattan), containing 1,050 beds and 102 bassinets, is the first general care facility completed in the city's 200-million-dollar post-World War II construction program. Metropolitan Hospital is affiliated with New York Medical College, Flower and Fifth Avenue Hospitals and, with these institutions and the new Bird S. Coler Memorial Hospital and Home on Welfare Island, comprises the New York Medical College-Metropolitan Medical Center. In addition to providing all medical and surgical services, the new center has a premature center of 40 bassinets, a contagious disease service of 36 beds, a tuberculosis service of 280 beds, and a division of physical medicine and rehabilitation. The largest wards in the hospital have only eight beds.

Personal.—Dr. Emil Froeschels has been elected honorary president of the Austrian Society for Speech and Voice Therapy. ——Dr. Benjamin W. Warner delivered a paper on "The Role of the Proctologist in the Diagnosis of Schistosomiasis Mansoni by Sigmoidoscopy and Rectal Biopsy" before the American Society of Tropical Medicine and Hygiene at the annual meeting in Boston Nov. 4.——Dr. Emilian A. Gutheil, editor of the *American Journal of Psychotherapy,* discussed "Obsession, Compulsion and Delusion" before the hospital staff of the Veterans Administration Hospital at Northport, Long Island, Oct. 26. ——Dr. Harvey J. Tompkins, director, Jacob L. Reiss Mental Health Pavilion of St. Vincent's Hospital of the City of New York, has been elected chairman of the professional advisory committee of the National Association for Mental Health. Dr. Tompkins is clinical professor of psychiatry at the Georgetown University School of Medicine in Washington, D. C., and until recently was director of the Psychiatry-Neurology Service of the Veterans Administration.——Dr. Currier McEwen is one of eight physicians invited by the World Health Organization to act as an advisory group to the Egyptian Ministry of Health. They will also serve as visiting faculty to the two medical schools in Cairo and the school in Alexandria. At the completion of the Egyptian meeting, Dr. McEwen will spend two weeks in France and Germany visiting arthritis and rheumatism research centers. ——Dr. Jean A. Curran, associate executive dean for medical education of the State University of New York College of Medicine at New York City, Brooklyn, is on a three months' leave of absence to conduct a survey of medical education in the Philippine Islands for the World Health Organization. En route to Manila Dr. Curran planned to visit WHO headquarters in Geneva, Switzerland; the Vellore Medical College, Madras, India; and Hong Kong, China, where a conference is scheduled with the dean and vice-chancellor of the University of Hong Kong. He plans to return to the United States via Formosa, Japan, Korea, and the Hawaiian Islands. At the request of the surgeon general of the U. S. Army, Dr. Curran will visit the army hospitals in Tokyo and in Honolulu.

OHIO

Pediatric Convulsive Disorders.—At the meeting of the Cincinnati Society of Neurology and Psychiatry in the Cincinnati Sanitarium, 5642 Hamilton Ave., Jan. 18, 8 p. m., "Some Aspects of Convulsive Disorders in Infancy and Childhood" will be considered by Dr. Gilbert B. Forbes, associate professor of pediatrics, University of Rochester (N. Y.) School of Medicine and Dentistry. The program is open to all physicians.

PENNSYLVANIA

Dr. Chapman Honored.—Dr. Leroy E. Chapman, Warren, state senator, has been awarded the Order of Merit, Carlos J. Finlay, by the Republic of Cuba. The Order of Finlay was conferred with the degree of Comendador.

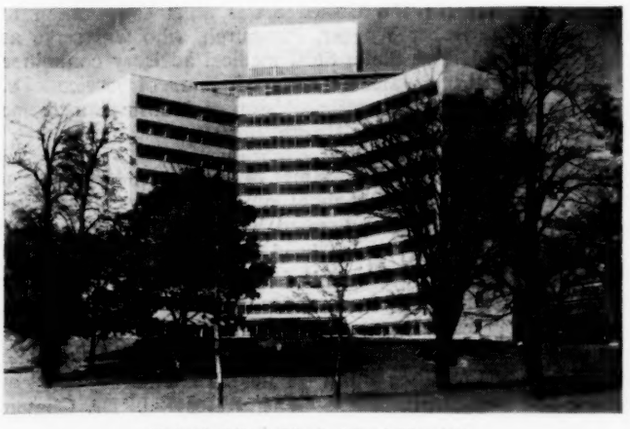
University News.—Dr. Carroll F. Burgoon Jr. has been appointed head, department of dermatology and syphilology, at Hahnemann Medical College and Hospital of Philadelphia. Dr. Burgoon, who lives in Conshohocken, maintains offices in Philadelphia and in Norristown.

Names of 273 Centenarians.—The Medical Society of the State of Pennsylvania requests that the names of Pennsylvania residents who will celebrate their 100th birthday during 1956 be sent, together with date of birth and address, to the society headquarters at 230 State St., Harrisburg. In accordance with a nine-year custom, each centenarian will receive a hand-lettered and framed testimonial. At last report, 273 such testimonials had been presented by officers of the medical societies of the counties in which the elderly persons live. During 1955, 28 centenarians were honored, and in most instances the elderly person's family doctor took part in the presentation ceremony.

Personal.—The board of trustees of the Tuberculosis League of Pittsburgh recently gave a reception for Dr. C. Howard Marcy in recognition of his 40 years of service to the league. Dr. Marcy, clinical professor of medicine at the University of Pittsburgh School of Medicine and lecturer at the Graduate School of Public Health, has served as consultant on staffs of several hospitals and is an area consultant in tuberculosis of the Veterans Administration. He is a former president of the Pennsylvania Tuberculosis and Health Society.——Dr. Jan Lieben of Boston has been appointed director of the bureau of industrial hygiene, Pennsylvania Department of Health. Dr. Lieben has been associated with the New York City Department of Health and the Connecticut State Department of Health. He succeeds Dr. Joseph Shilen, who has become chief of preventive medicine and occupational diseases at Olmsted Air Base, Middletown. ——Dr. Elmer Hess, Erie, President of the American Medical Association, was elected trustee-at-large to the National Society for Crippled Children and Adults at the Easter Seal Society's annual convention, Nov. 28-30, 1955, in Chicago (THE JOURNAL, Nov. 26, 1955, page 1315).

RHODE ISLAND

Addition to Rhode Island Hospital.—The 8-million-dollar Main Building of the Rhode Island Hospital, Providence, was dedicated Nov. 30. The new 10-story hospital has a capacity of 452 beds, 14 operating rooms, an x-ray department, laboratories,



Main Building, Rhode Island Hospital.

and many ancillary services. Each of the patient floors is assigned to a different medical service, with variations in its construction for the particular needs of that service. There are no large open wards, all patients being accommodated either in single rooms or in four-bed rooms. The Rhode Island Hospital, which was opened Oct. 1, 1868, with accommodations for 60 patients, now has facilities for 659 bed patients. Further development plans include a modern type of cancer research building, the construction of which is scheduled for the near future.

TENNESSEE

University News.—Vanderbilt University School of Medicine, Nashville, recently received a continuing annual scholarship of $1,000 from the Life and Casualty Insurance Company, Nashville, which announced that the program was launched in the interest of better public health and as part of the company's civic responsibility to make it economically possible for students of promise to complete their medical education. The scholarships are given on the condition that the recipient assumes the moral obligation of providing a similar scholarship.——The division

of physiology, University of Tennessee Medical Units, Memphis, announces that Donald B. Zilversmit, Ph.D., associate professor, is at the Mayo Clinic continuing his studies of liver function and phospholipids; C. Riley Houck, Ph.D., associate professor, has received grants totaling $16,092 in support of his studies on the mechanism of hypertension in nephrectomized animals; and Dr. Douglas A. Ross, assistant professor, is investigating the clinical uses of isotopes at Oak Ridge. J. P. Quigley, Ph.D., professor, was appointed to the newly developed radiation study section of the U. S. Public Health Service, and Dr. Jack Greenfield of Memphis has been made an instructor in physiology.—— A new $878,000 Administration-Postgraduate Building for the University of Tennessee Medical Units has been added to Memphis' Medical Center, and a $900,000 expansion has been announced. The new building is air-conditioned throughout. The expansion program will provide seventh and eighth floors for the Institute of Pathology Building; a fifth floor for the Pharmacy Building; and modernization of the C. P. J. Mooney Memorial Library Building. Completion of these projects will complete the 1951 building program of 5 million dollars, authorized by the Tennessee legislature.

WASHINGTON

Alfred Strauss Lecture.—Dr. Frederick A. Coller, professor of surgery, University of Michigan Medical School, Ann Arbor, will give the sixth Alfred A. Strauss Lecture Jan. 20, 8:15 p. m., at the University of Washington School of Medicine, Seattle. Dr. Coller will speak under the sponsorship of the department of surgery on "The Relation of Science to Surgery."

WISCONSIN

University News.—Dr. Leo Kanner, professor of psychiatry and pediatrics, Johns Hopkins University School of Medicine, Baltimore, will serve as Knapp Visiting Professor at the University of Wisconsin, Madison, during the second semester of the current academic year. He will teach in the medical school and will deliver several public lectures and lead discussions on child behavior. He is on the editorial boards of the *American Journal of Psychiatry, Archives of Criminal Psychodynamics,* the *Quarterly Journal of Child Behavior,* and the *Journal of Clinical and Experimental Psychopathology.*

GENERAL

Meeting on Clinical Research.—The annual meeting of the southern section of the American Federation for Clinical Research will convene at the Jung Hotel, New Orleans, at 9 a. m., Jan. 20. More than 40 speakers will participate by invitation. Dr. John H. Moyer, Houston, Texas, will preside.

Meeting on Geographical Pathology.—The International Society of Geographic Pathology, which will hold its sixth congress in Paris, France, in 1957 (July or September) will welcome participation by investigators from America. The subject for the conference will be "The Geographic Pathology of Peptic Ulcer." Information may be obtained from Dr. William B. Wartman, Secretary, American Section, International Society of Geographic Pathology, Northwestern University Medical School, 303 E. Chicago Ave., Chicago 11.

Annual Memorial Lectureship.—The American Gastroenterological Association has established the Memorial Lecture of the American Gastroenterological Association in memory of the departed members of the association. The lectureship was initiated at the annual scientific session June 4, 1955, in Atlantic City, N. J., by Dr. F. Avery Jones of London, England, whose subject was "Hematemesis and Melena." The following rotating committee is responsible for the selection of the annual lecturer: Dr. Jacob A. Bargen, Rochester, Minn., chairman, three years; Dr. Charles A. Flood, New York, two years; and Dr. Thomas E. Machella, Philadelphia, one year.

Cancer Cytology Congress.—At the annual meeting in Houston, Texas, Nov. 13, 1955, the Southern Society of Cancer Cytology adopted a resolution whereby it agreed to be the originating sponsor of the first Pan American Cancer Cytology Congress, "with the proviso that no financial obligation is incurred in such sponsorship." The congress, which is scheduled to be held in Miami, Fla., April 2-6, 1957, has received financial grants or pledges of aid from the Cancer Cytology Foundation of America, Inc., New York, Public Health Foundation for Cancer and Blood Pressure Research, Inc., Stamford, Conn., and the Williams Foundation of Buenos Aires, Argentina. Dr. J. Ernest Ayre, Miami, Fla., was named president of the first Pan American Congress of Cancer Cytology.

Conference of Radiologists.—The Eastern Conference of Radiologists will meet at the Lord Baltimore Hotel in Baltimore March 15-17, 1956. This informal organization, which has convened annually for more than 40 years, holds meetings in Boston, Baltimore, New York, Philadelphia, and Washington in that rotation, with the New England Roentgen Ray Society, the radiological section of the Baltimore City Medical Society, the New York Roentgen Ray Society, the Philadelphia Roentgen Ray Society, and the radiological section of the District of Columbia Medical Society acting as hosts and planning the program. There is no formal membership. Continuity is assured by a permanent secretary and an annual meeting of delegates. There are no commercial exhibits, but commercial representatives may register and sponsor activities either before or after the meeting. Advance registration may be made by writing to Dr. Richard B. Hanchett, 705 Medical Arts Building, Baltimore 1.

International Congress of Otolaryngology.—The sixth International Congress of Otolaryngology will take place in Washington, D. C., May 5-10, 1957, under the presidency of Dr. Arthur W. Proetz, St. Louis. The subscription for members is $25, which will include all official meetings of the congress except the banquet. Relatives accompanying members may be registered as associates at a fee of $10. The selected subjects for the plenary sessions to be held Monday, Wednesday, and Friday mornings will be: (1) chronic suppuration of the temporal bone, (2) collagen disorders of the respiratory tract, and (3) papilloma of the larynx. Two types of communications are invited: (1) contributions to the discussions of the selected subjects, limited to 5 minutes, and (2) original papers, limited to 15 minutes. These should be in one of the four official languages: English, French, German, Spanish. For information address the General Secretary, Dr. Paul H. Holinger, 700 N. Michigan Ave., Chicago 11.

Documentation Conference.—Western Reserve University, Cleveland, will hold a conference Jan. 16-18 on practical utilization of recorded knowledge for business, government, and professional people to determine how to handle the quantities of material that should be kept for future use in research and planning. Topics include: research and the decision-making process; ways in which research workers, executives, and others use information; inventorying and evaluating existing systems for analysis, storage, and retrieval of information; cooperative information processing; present state of educational programs for training of librarians, documentalists, and information specialists; characteristics of recorded information; and system of documentation terminology. During a panel discussion, "Cooperative Information Processing—Prospectus," Dr. Sanford V. Larkey, Welch Medical Library, Johns Hopkins University, Baltimore, will speak for medicine. Registration for the conference ($10 per person; $2.50 for students) includes preprints. Registrations are being handled by the Office of the Dean, School of Library Science, Western Reserve University, Cleveland 6.

Society News.—After confining its activities for 21 years to the states of Illinois, Missouri, and Iowa, the **Mississippi Valley Medical Society** is expanding to include Minnesota and Wisconsin. At the annual meeting the society chose the following officers: president, Dr. Frank R. Peterson, Cedar Rapids, Iowa; president-elect, Dr. George E. Kirby, Spring Valley, Ill.; vice-presidents, Drs. C. M. Zukerman, Davenport, Iowa; W. W. Fullerton, Sparta, Ill.; George T. Gafney, St. Louis; Waltman Walters, Rochester, Minn.; and Arnold S. Jackson, Madison, Wis.; secretary-treasurer (22nd year), Dr. Harold Swanberg, Quincy, Ill.; assistant secretary-treasurer, Dr. J. E. Reisch,

Springfield, Ill.; and accounting officer, Dr. Douglas M. Gover, Springfield, Ill. The 21st annual meeting will be held at the Hotel Morrison, Chicago, Sept. 26-28. The American Medical Writers' Association will hold its annual meeting at the same hotel Sept. 28-29.——The **Southern Medical Association** recently elected Dr. John P. Culpepper Jr., Hattiesburg, Miss., president-elect; Dr. Willis K. West, Oklahoma City, first vice-president; and Dr. Charles Denton Kerr, Houston, Texas, second vice-president.——Newly elected officers of the **American Society for the Study of Arteriosclerosis** include: Dr. Arthur C. Corcoran, Cleveland, president; Dr. Charles F. Wilkinson Jr., New York, vice-president; and Dr. O. J. Pollak, Dover, Del., secretary-treasurer.——Newly elected officers of the **Association of Medical Illustrators** include: Mr. Leon Schlossberg, Baltimore, president; Miss Eleanor A. Sweezey, Montreal, Canada, recording secretary; Miss Elizabeth Cuzzort, Brooklyn, treasurer; Miss Rose M. Reynolds, Omaha, corresponding secretary; and Mr. A. Hooker Goodwin, Chicago, vice-president.——Newly elected officers of the **American Academy of Neurological Surgery** include: Dr. Stuart N. Rowe, Pittsburgh, president; Dr. Jess D. Herrmann, Oklahoma City, vice-president; and Dr. Eben Alexander Jr., Winston-Salem, N. C., secretary-treasurer. The 1956 annual meeting will be held Oct. 31-Nov. 3 at the Camelback Inn, Phoenix, Ariz.——**Phi Delta Epsilon,** national medical fraternity, held its 51st annual convention Dec. 28-31 in Detroit. At the clinic in obstetrics and gynecology at Sinai Hospital, Dr. Abraham F. Lash, Chicago, discussed "Clinical Carcinoma in Pregnancy" and Dr. Henry C. Falk, New York, "Genitourinary Injuries Following Gynecological Surgery." Participants in a panel discussion on cardiovascular diseases that may be remedied by surgery included Drs. Paul S. Barker and Herbert E. Sloan of the University of Michigan Medical School, Ann Arbor, Drs. Robert F. Ziegler and Conrad R. Lam of Henry Ford Hospital, and Dr. Saul Rosenzweig of Sinai Hospital. The distinguished service award for 1955 was presented to Dr. Thomas Francis Jr., Ann Arbor, Mich., at the banquet.

LATIN AMERICA

Gastroenterologists Meet in Havana.—The fifth Pan American Congress of Gastroenterology and the sixth annual meeting of the Sociedad Cubana de Gastroenterologia will be held in Havana, Cuba, Jan. 20-27, under the auspices of Sociedad Interamericana de Gastroenterologia and Sociedad Cubana de Gastroenterologia. The following round tables have been scheduled: "Cirrhosis of the Liver," "Recent Advances in Gastroenterology," "Esophagus," and "Biliary Tract and Pancreas."

FOREIGN

Seminar Congresses in Otorhinolaryngology.—In its seminar congresses in otorhinolaryngology the American Medical Society of Vienna, Austria, will present the following programs by the medical faculty of the University of Vienna:

Feb. 2-4, Conservative Treatment of Acute and Chronic Otitis Media; New Aspects in Operative Treatment of Acute Sinusitis.

March 1-3, Anatomy of Temporal Bone; Tympanoplasty; Technique of Mobilization.

April 3-5, Neuro-otologic Diseases and Their Presurgical Aspects; Speech Rehabilitation with Special Reference to Laryngectomized Patients; Anatomy of the Facial Nerve Trauma; Operative Approach and Repair.

May 2-4, Anatomy of the Temporal Bone; Surgical Anatomy of the Nose; Surgical Anatomy of the Sinuses.

June 6-8, Nasal Allergy; Pediatric Otolaryngology; Surgical Treatment of the Parotid Glands.

July 4-6, Bronchoesophagology; Endoscopy; Malignant Disease in Otorhinolaryngology.

Aug. 1-3, Operative Otology; Surgical Treatment of the Larynx; Surgical Treatment of the Neck.

Sept. 5-7, Fenestration; Tympanoplasty; Rehabilitation of the Hard of Hearing.

Oct. 3-5, Surgical Treatment of the Nasal Septum; Reconstructive Surgery of the Nose and Ear; Cosmetic Surgery on Head and Neck.

Nov. 7-9, Acute Sinusitis; Chronic Rhinitis; Surgical Anatomy of Nose and Accessory Sinuses.

Details may be obtained from the American Medical Society of Vienna, Vienna I. Universitaetsstrasse 11. Cable: "Ammedic" Vienna.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1956 Annual Meeting, Chicago, June 11-15.

1956 Clinical Meeting, Seattle, Nov. 27-30.

1957 Annual Meeting, New York, June 3-7.

1957 Clinical Meeting, Philadelphia, Dec. 3-6.

1958 Annual Meeting, San Francisco, June 23-27.

ANNUAL CONGRESS ON INDUSTRIAL HEALTH, Sheraton-Cadillac Hotel, Detroit, Jan. 23-24. Mr. Clark D. Bridges, 535 N. Dearborn St., Chicago 10, Acting Secretary.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE, Palmer House, Chicago, Feb. 11-14. Dr. Edward L. Turner, 535 N. Dearborn St., Chicago 10, Secretary.

NATIONAL CONFERENCE ON RURAL HEALTH, Multnomah Hotel, Portland, Ore., Mar. 8-10. Mrs. Arline Hibbard, 535 N. Dearborn St., Chicago 10, Secretary.

ALASKA TERRITORIAL MEDICAL ASSOCIATION, Alaska Native Health Service Hospital, Anchorage, Feb. 20-22. Dr. Robert B. Wilkins, 1121 Fourth Ave., Anchorage, Secretary.

AMERICAN ACADEMY OF ALLERGY, Chase Hotel, St. Louis, Feb. 6-8. Dr. Francis C. Lowell, 65 East Newton St., Boston, Secretary.

AMERICAN ACADEMY OF OCCUPATIONAL MEDICINE, Netherlands-Plaza Hotel, Cincinnati, Feb. 15-17. Dr. Leonard J. Goldwater, 600 W. 168th St., New York 32, Secretary.

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS, Palmer House, Chicago, Jan. 28-Feb. 2. Dr. John R. Norcross, 122 South Michigan Blvd., Chicago 3, Secretary.

AMERICAN COLLEGE OF RADIOLOGY, Drake Hotel, Chicago, Feb. 10-11. Mr. William C. Stronach, 20 North Wacker Drive, Chicago 6, Executive Secretary.

AMERICAN SOCIETY FOR SURGERY OF THE HAND, Chicago, Jan. 27. Dr. George V. Webster, 1145 East Green St., Pasadena 1, Calif., Secretary.

CENTRAL SURGICAL ASSOCIATION, Hotel Kahler, Rochester, Minn., Feb. 23-25. Dr. Charles D. Branch, 102 North St., Peoria, Ill., Secretary.

CHICAGO MEDICAL SOCIETY ANNUAL CLINICAL CONFERENCE, Palmer House, Chicago, Feb. 28-March 1. Dr. Norris J. Heckel, 86 E. Randolph St., Chicago 1, Secretary.

DALLAS SOUTHERN CLINICAL SOCIETY, Dallas, Tex., Mar. 12-14. Miss Helga Boyd, 433 Medical Arts Bldg., Dallas 1, Tex., Executive Secretary.

MEDICAL SOCIETY EXECUTIVES CONFERENCE, Drake Hotel, Chicago, Feb. 6-8. Mr. H. Martin Baker, 1102 South Hillside, Wichita 17, Kansas, Secretary.

MICHIGAN CLINICAL INSTITUTE, Sheraton-Cadillac Hotel, Detroit, Mar. 7-9. Dr. L. Fernald Foster, 606 Townsend St., Lansing 15, Secretary.

MIDDLE SECTION, AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, Netherland Plaza, Cincinnati, Jan. 16. Dr. William H. Craddock, 2328 Auburn Ave., Cincinnati 19, Vice President.

NEUROSURGICAL SOCIETY OF AMERICA, Hotel Key Biscayne, Key Biscayne, Miami, Fla., Jan. 18-21. Dr. Lester A. Mount, 700 West 168th St., New York 32, Secretary.

NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, New Orleans, Feb. 27-March 1. Dr. Eugene H. Countiss, Room 103, 1430 Tulane Ave., New Orleans 12, Director.

NORTHWEST SOCIETY FOR CLINICAL RESEARCH, University of Oregon Medical School, Portland, Ore., Jan 21. Dr. Arthur L. Rogers, 1216 S.W. Yamhill St., Portland 5, Ore., Secretary.

REGIONAL MEETINGS, AMERICAN COLLEGE OF PHYSICIANS:

PHILADELPHIA, Jan. 27. Dr. Thomas M. McMillan, 330 South 9th St., Philadelphia 7, Governor.

SASKATOON, SASK., Feb. 3-4. Dr. C. H. A. Walton, Winnipeg Clinic, Winnipeg, Man., Canada, Governor.

TUCSON, ARIZ., Feb. 11. Dr. Leslie R. Kober, 15 East Monroe St., Phoenix, Ariz., Governor.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS:

JACKSONVILLE, FLA., Hotel George Washington, Jan. 16-18. Dr. Kenneth A. Morris, 2522 Oak St., Jacksonville 4, Fla., Chairman.

PHILADELPHIA, The Bellevue-Stratford, Feb. 13-16. Dr. Calvin M. Smyth Jr., Abington Memorial Hospital, Abington, Pa., Chairman.

MILWAUKEE, Hotel Schroeder, Feb. 27-29. Dr. Forrester Raine, 425 E. Wisconsin Ave., Milwaukee 4, Chairman.

COLORADO SPRINGS, COLO., The Broadmoor, Mar. 5-7. Dr. George W. Bancroft, 106 E. St. Vrain St., Colorado Springs, Colo., Chairman.

LITTLE ROCK, ARK., Hotel Marion, Mar. 12-13. Dr. Joseph F. Shuffield, 103 E. 7th St., Little Rock, Ark., Chairman.

SOCIETY OF UNIVERSITY SURGEONS, Hotel Claypool, Indianapolis, Feb. 8-10. Dr. C. Rollins Hanlon, 1325 South Grand Blvd., St. Louis 4, Secretary.

SOUTH ATLANTIC ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS, Hollywood Beach Hotel, Hollywood, Fla., Jan. 28-Feb. 1. Dr. C. H. Mauzy, Bowman Gray School of Medicine, Winston-Salem, N. C., Secretary.

SOUTHEASTERN SURGICAL CONGRESS, John Marshall Hotel, Richmond, Va., Mar. 12-15. Dr. Benjamin T. Beasley, 701 Hurt Bldg., Atlanta 3, Ga., Secretary.

SOUTHERN SECTION, AMERICAN FEDERATION FOR CLINICAL RESEARCH, Jung Hotel, New Orleans, Jan. 20. Dr. John H. Moyer, 1200 M. D. Anderson Blvd., Houston, Texas, Secretary.

SOUTHERN SECTION, AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, The Shamrock, Houston, Texas, Jan. 27-28. Dr. J. M. Robison, 1304 Walker Ave., Houston 2, Texas, Chairman.

U. S. SECTION, INTERNATIONAL COLLEGE OF SURGEONS, REGIONAL MEETING, Greenbrier Hotel, White Sulphur Springs, W. Va., Feb. 12-15. Dr. E. G. Gill, 711 South Jefferson St., Roanoke, Va., Chairman.

WESTERN SECTION, AMERICAN FEDERATION FOR CLINICAL RESEARCH, Golden Bough Theater, Carmel, Calif., Jan. 26. Dr. Charles M. Grossman, 301 Selling Bldg., Portland 5, Ore., Secretary.

WESTERN SECTION, AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, County Medical Society Bldg., San Francisco, Jan. 21. Dr. David D. DeWeese, 1216 S. W. Yamhill St., Portland, Ore., Vice President.

WESTERN SOCIETY FOR CLINICAL RESEARCH, Carmel-by-the-Sea, Calif., Jan. 27-28. Dr. Arthur J. Seaman, University of Oregon Medical School, Portland 1, Ore., Secretary.

FOREIGN AND INTERNATIONAL

ASSOCIATION OF INDUSTRIAL MEDICAL OFFICERS, London School of Hygiene and Tropical Medicine, London W.C.1, England, Sept. 24-28, 1956. Dr. J. A. A. Mekelburg, Peek, Frean and Company, Ltd., Keetons Rd., Bermondsey, London, S.E.16, England, Honorable Secretary.

BRITISH MEDICAL ASSOCIATION, Brighton, England, July 9-13, 1956. Dr. Angus Macrae, B. M. A. House, Tavistock Square, London, W.C.1, England.

CANADIAN MEDICAL ASSOCIATION, Quebec, P. Q., Canada, June 10-14, 1956. Dr. Arthur D. Kelly, 150 St. George St., Toronto 5, Ont., Canada, Secretary.

CONFERENCE OF INTERNATIONAL UNION FOR HEALTH EDUCATION OF THE PUBLIC, Rome, Italy, April 27-May 5, 1956. Mr. Lucien Viborel, 92 rue St. Denis, Paris 1er, France, Secretary-General.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Miami Beach, Fla., U.S.A., April 9-12, 1956. For information write: Dr. R. J. Whitacre, 13951 Terrace Road, Cleveland 12, Ohio, U. S. A.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LIMNOLOGY, Helsinki, Finland, July 26-Aug. 7, 1956. For information address: Dr. H. Luther, Snellmansgatan 16 C 36, Helsinki, Finland.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LOGOPEDICS AND PHONIATRICS, Barcelona, Spain, Sept. 3-7, 1956. Dr. J. Perello, Provenza 319, Barcelona 9, Spain, Secretary-General.

CONGRESS OF INTERNATIONAL SOCIETY OF HEMATOLOGY, Hotel Somerset, Boston, Mass., U.S.A., Aug. 27-Sept. 1, 1956. Dr. W. C. Moloney, 39 Bay State Road, Boston, Mass., U.S.A., Secretary.

CONGRESS OF LATIN SOCIETY OF OPHTHALMOLOGY, Madrid, Spain, April 24-28, 1956. For information address: Dr. Costi, Montalban 3, Madrid, Spain.

EUROPEAN CONGRESS OF ALLERGOLOGY, Florence, Italy, Sept. 12-15, 1956. Prof. Umberto Serafini, Instituto de Patologia Medica, Viale Morgagni, Florence, Italy, Secretary-General.

EUROPEAN CONGRESS OF CARDIOLOGY, Stockholm, Sweden, Sept. 10-14, 1956. Dr. Karl Erik Grewin, Sodersjukhuset, Stockholm, Sweden, General Secretary.

EUROPEAN SYMPOSIUM ON VITAMIN B_{12}, Hamburg, Germany, May, 1956. For information write: Doz. Dr. H. Bauer, Nervenklinik, Hamburg-Eppendorf, Germany.

HEALTH CONGRESS, ROYAL SOCIETY FOR THE PROMOTION OF HEALTH, Blackpool, England, April 24-27, 1956. Mr. P. Arthur Wells, 90 Buckingham Palace Road, London S.W. 1, England, Secretary.

INTER-AMERICAN CONGRESS OF CARDIOLOGY, Havana, Cuba, Nov. 4-10, 1956. For information address: Dr. Ramon Aixala, Apartado 2108, Havana, Cuba.

INTERNATIONAL ACADEMY OF PATHOLOGY, Cincinnati, Ohio, U. S. A., April 24-25, 1956. Dr. F. K. Mostofi, Armed Forces Institute of Pathology, Washington 25, D. C., U. S. A., Secretary.

INTERNATIONAL CONGRESS AGAINST ALCOHOLISM, Istanbul, Turkey, Sept. 10-15, 1956. For information address: International contre l'Alcoolisme, Case Gare 49, Lausanne, Switzerland.

INTERNATIONAL CONGRESS ON ANIMAL REPRODUCTION, Arts School, University of Cambridge, Cambridge, England, June 25-30, 1956. Dr. Joseph Edwards, Production Division, Milk Marketing Board, Thames Ditton, Surrey, England, Hon. Secretary.

INTERNATIONAL CONGRESS OF ANTHROPOLOGICAL AND ETHNOLOGICAL SCIENCES, Philadelphia, Pa., U. S. A., Sept. 2-9, 1956. Dr. William N. Fenton, National Research Council, Division of Anthropology and Psychology, 2101 Constitution Avenue, Washington 25, D. C., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF DIETETICS, Congress Palace, Esposizione Universale Roma, Rome, Italy, Sept. 10-14, 1956. Prof. E. Serianni, Associazione Dietetica, Italiana, via dei Penitenzieri N. 13, Rome, Italy, Secretary General.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Cologne, Germany, Aug. 19-23, 1956. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, U. S. A., Executive Director.

INTERNATIONAL CONGRESS OF ENTOMOLOGY, Montreal, Canada, Aug. 17-25, 1956. Mr. J. A. Downes, Science Service Bldg., Carling Ave., Ottawa, Ont., Canada, Secretary.

INTERNATIONAL CONGRESS OF GASTROENTEROLOGY, London, England, July 18-21, 1956. Mr. Hermon Taylor, London Hospital, White Chapel, London E.1, England, Honorable Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Maison de la Mutualite, Paris, France, June 5-8, 1956. For information address: Mr. M. H. Thoillier, 37 Rue de Monthlon, Paris 9e, France.

INTERNATIONAL CONGRESS FOR THE HISTORY OF SCIENCE, Florence and Milan, Italy, Sept. 3-10, 1956. Dr. M. L. Bonelli, Instituto di Ottica, Arcetri, Florence, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF HUMAN GENETICS, Copenhagen, Denmark, Aug. 1-6, 1956. For information address: The University Institute for Human Genetics, Tagensvej 14, Copenhagen N, Denmark.

INTERNATIONAL CONGRESS OF HYDATID DISEASE, Athens, Greece, Sept. 14-18, 1956. Prof. B. Kourias, Croix-Rouge Hellenique, 1 rue Mackenzie King, Athens, Greece, Secretary-General.

INTERNATIONAL CONGRESS ON INFECTIOUS PATHOLOGY, Lyon, France, May 24-26, 1956. General Secretariat: Institut Pasteur de Lyon, 77 rue Pasteur, Lyon, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Madrid, Spain, Sept. 19-23, 1956. Dr. J. C. De Oya and Dr. J. Gimena, Hostaleza No. 90, Madrid, Spain, Secretaries.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Palmer House, Chicago, Illinois, U. S. A., Sept. 9-13, 1956. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF NEO-HIPPOCRATIC MEDICINE, Montecatini, Terme, Italy, May 20-22, 1956. Dr. Valente, 41 Avenue Verdi, Montecatini Terme, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Copenhagen, Denmark, July 22-27, 1956. Professor P. Plum, Rigshospitalet, Copenhagen, Denmark, President.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, Copenhagen, Denmark, August 20-24, 1956. Dr. B. Strandberg, Kobenhavns amts sygehus i Gentofte, Dept. of Rheumatology and Physical Medicine, Hellerup, Denmark, Honorable Secretary.

INTERNATIONAL CONGRESS OF RADIOLOGY, Mexico, D. F., Mexico, July 22-28, 1956. Dr. Jose Noriega, Tepic 126 (2e piso), Mexico, D. F. 7, Mexico, Secretary General.

INTERNATIONAL CONGRESS OF WORLD CONFEDERATION FOR PHYSICAL THERAPY, Hotel Statler, New York, New York, U. S. A., June 17-23, 1956. For information address: Miss Mildred Elson, American Physical Therapy Association, 1790 Broadway, New York 19, New York, U. S. A.

INTERNATIONAL GENETICS SYMPOSIUM, Tokyo and Kyoto, Japan, Sept. 6-12, 1956. For information address: Secretary, International Genetics Symposium, Science Council of Japan, Ueno Park, Tokyo, Japan.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Brussels, Belgium, July 29-Aug. 5, 1956. For information address: Prof. J. Reuse, Faculte de Medicine et de Pharmacie, 115 Boulevard de Waterloo, Brussels, Belgium.

INTERNATIONAL PROFESSIONAL UNION OF GYNECOLOGISTS AND OBSTETRICIANS, Madrid, Spain, Sept. 28-29, 1956. Dr. Jacques Courtois, 1 rue Racine, St-Germain-en-Laye (S and O), France, Permanent International Secretary-General.

INTERNATIONAL SYMPOSIUM ON VENEREAL DISEASES AND THE TREPONEMATOSES, Hotel Statler, Washington, D. C., U. S. A., May 28-June 1, 1956. For information address: Dr. Charles A. Smith, Chief, Venereal Disease Program, Division of Special Health Services, Public Health Service, Dept. of Health, Education and Welfare, Washington 25, D. C., U. S. A.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, San Juan, Puerto Rico and Curacao, N.W.I., Jan. 29-Feb. 8, 1956. Dr. Cassius Lopez de Victoria, 176 East 71st St., New York 21, New York, U. S. A., Executive Director.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION, EXTRAORDINARY GENERAL ASSEMBLY, Burgenstock, Nidwalden, Switzerland, Sept. 21-23, 1956. Dr. Janet Aitken, 30a Acacia Road, London N.W. 1, England, Secretary.

MIDDLE EAST MEDICAL ASSEMBLY, Campus, American University of Beirut, Beirut, Lebanon, April 7-9, 1956. Dr. Virgil C. Scott, American University of Beirut, Beirut, Lebanon, Chairman.

NATIONAL CONGRESS OF PEDIATRICS, Cuidad Universitaria, Mexico D.F., Mexico, May 1-5, 1956. Dr. Ignacio Avila Cisneros, Calzada de Madereros No. 240, Mexico 18, D.F., Mexico, Coordinator.

NORTH QUEENSLAND MEDICAL CONFERENCE, Cairns, North Queensland, Australia, June 25-30, 1956. Dr. W. R. Horsfall, P. O Box 672, Cairns, N.Q., Australia, Secretary.

PAN-AMERICAN ACADEMY OF GENERAL PRACTICE, San Juan, Puerto Rico and Curacao, N.W.I., Jan. 29-Feb. 8, 1956. Dr. Arturo Martinez, 54 East 72d St., New York 21, New York, U. S. A., Secretary.

PAN AMERICAN CONGRESS OF GASTROENTEROLOGY, Havana, Cuba, Jan. 20-27, 1956. For information address: Dr. Norberto M. Stapler, 1267 J. E. Uriburu, Buenos Aires, Argentine, S. A.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, San Juan, Puerto Rico, April 8-12, 1956. Dr. C. E. Munoz MacCormick, Apartado 9111, Santurce 29, Puerto Rico, Secretary General.

PAN AMERICAN MEDICAL WOMEN'S ALLIANCE, Santiago, Chile, March 6-13, 1956. For information address: Dr. Eva Cutright, 458 Beall Ave., Wooster, Ohio, U. S. A.

WORLD CONGRESS ON FERTILITY AND STERILITY, Naples, Italy, May 18-26, 1956. Dr. Maxwell Roland, 114-20 Queens Boulevard, Forest Hills 75, New York, N. Y., U. S. A., Chairman, Liaison Committee.

WORLD MEDICAL ASSOCIATION, Havana, Cuba, Oct. 9-15, 1956. Dr. Louis H. Bauer, 345 East 46th St., New York 17, New York, U. S. A., Secretary-General.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Various Centers. April 24-25 (Part II); June 19-20 (Parts I and II); September 4-5 (Part I). Candidates may file applications at any time but they must be received at least six weeks before the date of the examination for which application is made. New candidates should apply by formal registration; registered candidates may notify the board, indicating desired location, date and candidate number. Ex. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 19-21. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

ARIZONA:* *Examination.* Phoenix, Jan. 18-19. *Reciprocity.* Phoenix, Jan. 21. Sec., Dr. M. R. Richter, 411 Security Bldg., Phoenix.

ARKANSAS:* *Examination.* Little Rock, June 14-15. Sec., Dr. Joe Verser, Harrisburg.

CALIFORNIA: *Examination.* Los Angeles, Feb. 27-Mar. 1. Sec., Dr. Louis E. Jones, 1020 N St., Room 436, Sacramento.

CONNECTICUT:* *Examination.* New Haven, March 12-14. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven.

DELAWARE: *Reciprocity.* Dover, Jan. 19. Sec., Dr. Joseph S. McDaniel, Dover.

DISTRICT OF COLUMBIA:* *Examination.* Washington, May 14-15. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N.W., Washington.

FLORIDA:* *Examination.* Miami Beach, June 24-26. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

GEORGIA: *Examination and Reciprocity.* Atlanta, June. Sec., Mr. Cecil L. Clifton, 111 State Capitol, Atlanta 3.

ILLINOIS: *Examination and Reciprocity.* Chicago, Jan. 24-26. Supt. of Regis., Mr. Frederic B. Selcke, Capitol Building, Springfield.

INDIANA: *Examination.* Indianapolis, June. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

MAINE: *Examination.* Portland, Mar. 13-14. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MASSACHUSETTS: *Examination.* Boston, Jan. 17-20. Sec., Dr. Robert C. Cochrane, Room 37, State House, Boston 33.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 13-15. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., Lansing.

MINNESOTA:* *Examination.* Minneapolis, Jan. 17-19. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

MONTANA: *Examination and Reciprocity.* Helena, April 3. Sec., Dr. S. A. Cooney, 7 West 6th Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June 18-20. Director, Bureau of Examining Boards, Mr. Husted K. Watson, 1009 State Capitol Bldg., Lincoln.

NEW HAMPSHIRE: *Examination and Endorsement.* Concord, March 14. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 19-22. Sec., Dr. Patrick H. Corrigan, 28 W. State St., Trenton.

NEW MEXICO:* *Examination and Endorsement.* Santa Fe, May 21-22. Sec., Dr. R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NEW YORK: *Examination.* Albany, Buffalo, Syracuse and New York, Feb. 7-10. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

NORTH CAROLINA: *Reciprocity.* Durham, Jan. 16. *Examination.* Durham, June 18-21. Sec., Dr. Joseph J. Combs, Professional Bldg., Raleigh.

OKLAHOMA:* *Examination.* Oklahoma City, June 5-6. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, Jan. 16-17. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PENNSYLVANIA: *Examination.* Philadelphia, Jan. 23-26. Acting Sec., Miss Marguerite G. Steiner, Box 911, Harrisburg.

SOUTH DAKOTA:* *Examination.* Sioux Falls, Jan. 17-18. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 18-20. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Reciprocity.* Salt Lake City, Feb. 21. *Examination.* Salt Lake City, July 11-13. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

VERMONT: *Examination.* Burlington, Jan. 25-27. Sec., Dr. F. J. Lawliss, Richford.

WISCONSIN:* *Reciprocity,* Madison, Spring; *Reciprocity and Examination.* Milwaukee, July 10-12. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

WYOMING: *Examination and Endorsement.* Cheyenne, Feb. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

ALASKA:* On application. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Sec., Dr. John E. Kennedy, Agana.

PUERTO RICO: *Examination.* San Juan, Mar. 6-10. Sec., Dr. Joaquin Mercado Cruz, Box 3271, San Juan.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: *Examination.* Little Rock, May 4-5. Sec., Mr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

CONNECTICUT: *Examination.* New Haven, Feb. 11. Address: State Board of Healing Arts, 258 Bradley St., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 23-24. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave. N.W., Washington 6.

FLORIDA: *Examination.* Miami, June 9. Sec., Mr. M. W. Emmel, Box 340, Gainesville.

MICHIGAN: *Examination.* Detroit and Ann Arbor, Feb. 10-11. Sec., Mrs. Anne Baker, 410 W. Michigan Ave., Lansing 15.

NEW MEXICO: *Examination.* Santa Fe, Jan. 15. *Reciprocity.* Sec., Mrs. Marguerite Cantrell, Box 1522, Santa Fe.

OKLAHOMA: *Examination and Reciprocity.* Oklahoma City, Mar. 30-31. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, March 3; June 2, Sept. 8 and Dec. 1. Dr. Earl M. Pallett, Sec., State Board of Higher Education, Eugene.

RHODE ISLAND: *Examination.* Providence, Feb. 15. Admin. of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

TENNESSEE: *Examination.* Memphis, Mar. 21-22. Sec., Mr. O. W. Hyman, 62 S. Dunlap St., Memphis 3.

TEXAS: *Examination.* Galveston, Dallas, and such other locations as are warranted, April. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: *Examination.* Madison, April 7 and Milwaukee, June 2. Final date for filing application is Mar. 30. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

ALASKA: On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

*Basic Science Certificate required.

MAGAZINE–TELEVISION REPORT

The following list of current medical articles in mass-circulation magazines and forthcoming network television programs on medical subjects is published each week only for the information of readers of THE JOURNAL. *Unless specifically stated, the American Medical Association neither approves nor disapproves of the articles and programs reported.*

TELEVISION

Monday, Jan. 23

NBC-TV, 9 p. m. EST. "Medic" shows how a man's life is saved by an operation on a pancreatic tumor in a teleplay titled "Just Like Your Father."

ABC-TV, 9:30 p. m. EST. "Medical Horizons" does a remote telecast on rehabilitation of cerebral palsy patients from the University of Rochester School of Medicine in New York.

MAGAZINES

Better Homes and Gardens, January, 1956

"The New Ambulance that Flies," by Dan Paonessa

Hospitals in Buffalo, N. Y., and Santa Monica, Calif., use helicopters to pick up emergency cases from isolated spots.

American Magazine, January, 1956

"Don't Be Afraid of Your Heart," by H. M. Marvin, M.D.

A heart specialist gives a factual summary of information on high blood pressure, atherosclerosis, and thrombosis in an effort to dispel fear aroused by recent publicity on heart ailments.

GOVERNMENT SERVICES

AIR FORCE

New Air Force Program for Medical Students.—The surgeon general announces a new Air Force training program that will provide a valuable educational subsidy of junior and senior medical students. A special announcement of the new program has been sent to the deans of all medical colleges and universities whose students are eligible to participate.

Air Force medical representatives will contact students during the coming month to make available information and application kits to those interested. Closing date for applications is March 1, 1956, and the program commences with the school year 1956-1957. Junior and senior students are eligible for appointment as second lieutenants in the medical component of the Air Force Reserve, with concurrent active duty at their schools, and will receive the pay and allowances of second lieutenants. On graduation, these students are eligible for reappointment as first lieutenants in the Medical Corps. Tuition and other school costs will be borne by the student officers.

The program represents the adoption of recommendations of the armed forces task force group appointed last June by the Secretary of Defense to explore solutions to the problem of providing greater career incentives for military medical officers.

NAVY

Correspondence Course in Atomic Medicine.—Atomic Medicine is the title of a new medical department correspondence course now ready for distribution to eligible regular and reserve officers and enlisted personnel of the medical department of the Navy. Evaluated at 24 promotion and retirement points, it consists of eight objective question type assignments. The textbook used for this course is a complete new revision of "Atomic Medicine," second edition, edited by Rear Adm. C. F. Behrens, M. C., U. S. N.

Applications for this course should be submitted on form NavPers 992 (with appropriate change in the "TO" line), and forwarded via appropriate channels to the Commanding Officer, U. S. Naval Medical School, Bethesda 14, Md. Regular and reserve personnel who have satisfactorily completed the previous course, Radiological Defense and Atomic Medicine, either the thesis or objective type, will receive additional credit for this course.

Anesthesiologists Urgently Needed.—The U. S. Navy Bureau of Medicine and Surgery urgently needs certified or board eligible anesthesiologists for service in various naval hospitals in continental United States. The bureau desires to correspond with or interview civilian specialists among the reserve components of the Navy Medical Corps (inactive) or those who have no military affiliations but may reasonably expect induction into the armed forces within the next 12 months under existing law, and others who might desire to consider applying for commission in the Naval Reserve for the purpose of performing extended active duty or for commission in the regular Navy for career purposes in anesthesiology. Communication should be directed to the Chief, Bureau of Medicine and Surgery, Department of the Navy, Washington 25, D. C.

VETERANS ADMINISTRATION

Personal.—Dr. Joseph B. Bounds, manager of the VA Hospital at Jefferson Barracks, Mo., has been appointed manager at the VA Hospital in Roanoke, Va., succeeding Dr. Charles W. Grady, who will retire. Dr. Bounds joined VA in 1939. From 1942 to 1946 he served with the U. S. Navy Medical Corps. On his separation as a commander in 1946, he returned to the North Little Rock VA Hospital, where he was chief of professional services until 1950. He was manager of the VA Hospital at Tomah, Wis., from 1950 to 1952, when he was appointed to his present position at Jefferson Barracks. He was certified by the American Board of Psychiatry and Neurology in 1948.

Hospital News.—Dr. Milton Rosenbaum, chairman, department of psychiatry, Albert Einstein College of Medicine, Yeshiva University, New York, addressed the staff of the VA Hospital at Northport, L. I., New York, Dec. 13 on "The Doctor's Relationship with Patients, with Emphasis on Psychosomatic Disorders."——Dr. Harold G. Wolff, professor of neurology, Cornell University Medical College, New York, addressed the staff of the Veterans Administration Hospital at Northport, N. Y., Dec. 9 on "Recent Advances in the Study of Headaches."

PUBLIC HEALTH SERVICE

International Symposium on Venereal Diseases.—The first International Symposium on Venereal Diseases and the Treponematoses will be held at the Statler Hotel, Washington, D. C., May 28-June 1, 1956, sponsored by the Public Health Service, and the World Health Organization. The symposium is expected to draw specialists from many countries of the world.

The agenda will cover: Control of Venereal Diseases and the Treponematoses in Retrospect and Prospect; Reporting and Statistical Problems; Natural History of Syphilis and the Treponematoses; Experimental Syphilis and the Treponematoses; Serology and Immunology of the Treponematoses; Diagnosis, Management, and Prognosis of the Treponematoses and the Venereal Diseases; Gonorrhea, the Minor Venereal Diseases, and Nongonococcic Urethritis; Epidemiology and Control Techniques; Health Education and Public Information; and Voluntary Agency Cooperation in Control Programs.

The symposium is open to all physicians, scientists, and professional health workers interested in participating. Anyone interested in submitting a paper for consideration by the program committee should send an abstract to Dr. C. A. Smith, Medical Director, Chief, Venereal Disease Program, Division of Special Health Services, Public Health Service, Washington 25, D. C., as soon as possible. Accepted papers may be presented in person or by an alternate. All abstracts to be considered for the program must be received no later than Feb. 1, 1956. The working languages of the symposium will be French, Spanish, and English.

Research on Air Pollution.—The Public Health Service has contracted with three federal agencies to conduct research in community air pollution problems. Congress last year appropriated $1,785,000 to the PHS for its air pollution research program this year. Under this program, the PHS has allocated $392,000 to the Bureau of Mines, the National Bureau of Standards, and the Weather Bureau.

Of this sum, $196,000 will be used by the Weather Bureau to study the dilution and dispersal of contaminants in the atmosphere. The National Bureau of Standards has been allocated $98,000 to develop methods of identifying various gaseous contaminants; for studies of methods for determining atmospheric content of various substances; for exploring methods of treating condensable pollutants; and for studying reactions that take place in air between gases and chemicals that may cause pollution of major importance.

The Bureau of Mines will investigate the causes of inadequate incineration of combustible wastes and the means of improving incineration; will evaluate elements from interval combustion in engines that may contribute to air-pollution; and will sample a limited number of stack effluents, among other studies. The PHS has allocated $98,000 to the Bureau of Mines for the current year.

DEATHS

Conley, Dudley Steele ⊕ Columbia, Mo.; born in Columbia Jan. 26, 1878; Columbia University College of Physicians and Surgeons, New York City, 1906; dean emeritus and professor emeritus of surgery at the University of Missouri School of Medicine, where he joined the faculty in 1919; upon his retirement, friends and former students joined the medical faculty in commissioning the painting of a portrait that was formally presented to the university in 1951; at one time on the faculty of his alma mater; member of the founders group of the American Board of Surgery; at one time president and vice-president of the Missouri State Medical Association; in 1935 president of the Boone County Medical Society; for one year vice-president of the Association of American Medical Colleges; fellow of the American College of Surgeons; formerly director of surgery at the University Hospitals; served during World War I; died Oct. 4, aged 77, of carcinoma.

Meissner, Tom Otto Walter ⊕ Athens, Ga.; born in Vienna, Austria, Aug. 3, 1911; Medizinische Fakultät der Universität, Vienna, Austria, 1936; interned at the Passavant Hospital in Pittsburgh; formerly a resident of the Baptist Hospital in Birmingham, Ala., and the Veterans Administration Hospital in Chamblee, Ga., where he was chief of the eye, ear, nose, and throat service; served during World War II; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Ophthalmology; certified by the National Board of Medical Examiners; died in an automobile accident Sept. 29, aged 44.

Cohen, Samuel E. ⊕ Binghamton, N. Y.; Universität Zurich Medizinische Fakultät, Switzerland, 1936; specialist certified by the American Board of Pathology; member of the College of American Pathologists and the American Society of Clinical Pathologists; fellow of the American College of Physicians; for many years associated with the Arnot-Ogden Memorial Hospital in Elmira; on the staffs of the Tioga County General Hospital in Waverly, Chemung County Sanatorium and Elmira Reformatory Hospital in Elmira, and Our Lady of Lourdes Memorial Hospital, where he died Nov. 9, aged 45, of coronary disease.

Ballard, Carsie Z. ⊕ Dublin, Miss.; Memphis (Tenn.) Hospital Medical College, 1909; died Nov. 25, aged 74.

Beatty, Edward Daniel ⊕ Mallard, Iowa; McGill University Faculty of Medicine, Montreal, Canada, 1895; died in Rochester, Minn., Oct. 19, aged 84, of cerebral infarction.

Boulton, Eleanore F. ⊕ Redding, Conn.; Woman's Medical College of Pennsylvania, Philadelphia, 1900; died Nov. 22, aged 82.

Buck, Margaret L. Muehlenbein ⊕ Chicago; Jenner Medical College, Chicago, 1914; member of the American Academy of General Practice; vice-president of the Illinois Academy of General Practice; on the staff of the South Chicago Hospital; died in the Mercy Hospital Nov. 3, aged 66, of carcinoma of the lungs.

Burt, Samuel Perry ⊕ Louisburg, N. C.; College of Physicians and Surgeons, Baltimore, 1896; served as health officer of Franklin County; died in the Franklin Memorial Hospital Oct. 14, aged 84, of hypostatic pneumonia and diabetes mellitus.

Candidus, Eugene William, Bronxville, N. Y.; Kentucky School of Medicine, Louisville, 1892; died in Ossining Sept. 13, aged 81, of arteriosclerotic heart disease.

Cantrell, Benjamin Casey ⊕ Plantersville, Miss.; University of Tennessee College of Medicine, Memphis, 1916; served on the staff of the North Mississippi Community Hospital in Tupelo; died Nov. 21, aged 70, of cancer of the liver.

⊕ Indicates Member of the American Medical Association.

Christian, Frank Lamar, Elmira, N. Y.; New York University Medical College, New York City, 1898; Cornell University Medical College, New York City, 1899; for many years superintendent of the Elmira Reformatory; served as president of the board of education of Elmira; died in Arnot-Ogden Hospital Oct. 18, aged 79, of aplastic anemia and bronchopneumonia.

Clayton, John Wesley ⊕ Johnston City, Ill.; St. Louis University School of Medicine, 1904; served as a member of the high school board and one term as city alderman; died Nov. 10, aged 80.

Clutz, Ralph Robertson, Bendena, Kan.; Kansas City (Mo.) Medical College, 1900; member of the Kansas Medical Society; served two terms as county health officer; died in Atchison Nov. 29, aged 78, of chronic leukemia and congestive heart disease.

Cole, Arthur Vincent ⊕ East Chicago, Ind.; Rush Medical College, Chicago, 1923; member of the Industrial Medical Association; charter member of the International College of Surgeons and fellow of the American College of Surgeons; on the staff of St. Catherine's Hospital, where he died Nov. 2, aged 57, of ruptured esophageal varicosity.

Dowd, Richard Edward, San Bernardino, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1908; specialist certified by the American Board of Otolaryngology; on the staff of St. Bernardine's Hospital; in 1949 was made a Knight of St. Gregory by Pope Pius XII; died Nov. 23, aged 77, of pulmonary edema.

Farrington, Paul Robert ⊕ Boulder, Colo.; Harvard Medical School, Boston, 1920; died Sept. 9, aged 60, of cancer of the liver.

Felts, Wylie Robert, Judsonia, Ark.; University of Tennessee College of Medicine, Memphis, 1914; member of the Arkansas Medical Society; served as mayor of Judsonia; World War I veteran; served as president of the school board; for many years director of the Farmers and Merchants Bank; died Nov. 17, aged 65.

Franz, Adolph ⊕ Holyoke, Mass.; College of Physicians and Surgeons, Medical Department of Columbia College, New York City, 1887; fellow of the American College of Surgeons; on the staffs of the Holyoke and Providence hospitals; died Nov. 22, aged 93, of arteriosclerotic myocarditis.

Hale, Robert Eugene ⊕ Bellamy, Ala.; Chattanooga (Tenn.) Medical College, 1904; served during the Spanish-American War and World War I; member of the American Academy of General Practice; past-president of the Sumter County Medical Society; on the staff of the Bellamy Hospital; died Oct. 24, aged 80.

Harris, Farley Wingfield, Birmingham, Ala.; Birmingham Medical College, 1909; member of the Medical Association of the State of Alabama; on the staffs of the South Highlands Infirmary and the University Hospital, where he died Sept. 10, aged 66, of cerebral vascular accident.

Harvey, Edward Regis, Seymour, Conn.; Baltimore Medical College, 1909; member of the Connecticut State Medical Society; for many years health officer for the town of Seymour; senior surgeon of the honorary medical staff at Griffin Hospital in Derby; consultant in surgery at the Hospital of St. Raphael in New Haven; died Nov. 5, aged 70, of coronary occlusion and myocardial infarction.

Hazen, Robert ⊕ Thomaston, Conn.; University of Vermont College of Medicine, Burlington, 1898; for many years a member of the board of education; formerly president of the Thomaston Savings Bank; on the consulting staff of Waterbury (Conn.) Hospital; died Nov. 1, aged 82, of cerebral hemorrhage and arteriosclerosis.

Henry, Ziba Lindley ✠ Colonel, U. S. Army, retired, San Francisco; Starling Medical College, Columbus, 1896; entered the regular Army as a major Sept. 9, 1920; his 35 years of service included World Wars I and II, the campaign against Pancho Villa in Mexico, and the 1909 expedition against the Moros in Mindanao; retired Nov. 17, 1943; died in the Letterman General Hospital Oct. 16, aged 82, of carcinoma of the head of the pancreas.

Hinnen, Gustave Augustus, Cincinnati; Miami Medical College, Cincinnati, 1904; died in the Jewish Hospital Nov. 22, aged 75.

Huey, Thomas Wang ✠ Jackson, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1894; died Nov. 15, aged 82, of cirrhosis of the liver.

Johnson, Robert Stanislaus ✠ Boston; Albany (N. Y.) Medical College, 1945; clinical instructor in psychiatry at Tufts College Medical School; certified by the National Board of Medical Examiners; interned at the Naval Hospital in Norfolk, Va.; served during World War II; affiliated with the Boston State Hospital; died in the Haynes Memorial Hospital of the Massachusetts Memorial Hospitals, Oct. 27, aged 34, of poliomyelitis.

Jones, Carl Thomas ✠ Newville, Ala.; University of Alabama School of Medicine, University, 1917; past-president of the Henry County Medical Association; served during World War I; died Sept. 15, aged 63, of cerebral hemorrhage.

Kirk, Arthur Alburtus ✠ Tuscaloosa, Ala.; Medical College of Alabama, Mobile, 1897; formerly health officer of Tuscaloosa County; served during World War I; died in the Druid City Hospital Nov. 24, aged 87.

Liechty, Ernest John, Kingsley, Iowa; Drake University College of Medicine, Des Moines, 1905; for many years health officer; member of the school board; died in the Mercy Hospital, Iowa City, Oct. 28, aged 76, of carcinoma of the rectum.

McCall, Daniel Thompson ✠ Mobile, Ala.; Louisville (Ky.) Medical College, 1894; fellow of the American College of Physicians; formerly member of the senate in the state legislature; served on the state board of education and the state board of health; on the staffs of the Providence Hospital and the Mobile Infirmary; died Nov. 9, aged 86, of coronary occlusion.

McDonald, Charles Wesley, Jacksonville, Fla.; University of Nashville (Tenn.) Medical Department, 1904; served as director of the Gadsden County Health Department with headquarters in Quincy; formerly director of county health work, Alabama State Department of Health; at one time practiced in Marianna, and was district health officer; died in St. Vincent's Hospital Oct. 1, aged 87, of arteriosclerotic heart disease.

MacLean, Sydney Murdoc ✠ South Daytona, Fla.; Washington University School of Medicine, St. Louis, 1907; member of the Washington State Medical Association; fellow of the American College of Surgeons; died Nov. 10, aged 75, of pulmonary tuberculosis.

Maddox, Robert Daniel ✠ Cincinnati; Medical College of Ohio, Cincinnati, 1900; fellow of the American College of Surgeons; member of the Association of Military Surgeons of the United States and the Academy of Medicine of Cincinnati; at one time lecturer on military medicine at the University of Cincinnati College of Medicine; served as superintendent of the City Hospital, Springfield, Ohio; during World War I professor of orthopedic surgery at the U. S. Army Medical School in Washington, D. C.; died Nov. 16, aged 79, of carcinoma of the liver.

Marxer, Barney Joseph ✠ Dupo, Ill.; St. Louis College of Physicians and Surgeons, 1908; past-president of St. Clair County Medical Society; president of the Dupo Building and Loan Association; on the staffs of the Missouri Pacific Railroad Hospital Association in St. Louis, and the Christian Welfare and St. Mary's hospitals in East St. Louis; died Nov. 16, aged 72, of coronary thrombosis.

Maxey, Nathaniel Coleman, Mountain View, Ark.; University of Arkansas School of Medicine, Little Rock, 1911; died in the Allen Hospital, Batesville, Sept. 10, aged 81.

Murrah, Frank Clay ✠ Herrin, Ill.; Rush Medical College, Chicago, 1910; twice president of the Williamson County Medical Society; member of the American Academy of General Practice; medical officer for the 16th Field Artillery in France and Germany during World War I; for many years owner of the Herrin Hospital; died in the Veterans Administration Hospital, Jefferson Barracks, Mo., Oct. 21, aged 74, of bronchopneumonia and cerebral arteriosclerosis.

Pattison, Charles G., Marthaville, La.; Memphis (Tenn.) Hospital Medical College, 1903; died Sept. 29, aged 79, of heart disease.

Pike, Charles Heyfield, Evanston, Ill.; University of Pennsylvania School of Medicine, Philadelphia, 1912; died Oct. 7, aged 69, of cancer.

Rosenkrans, Harvey R., Redkey, Ind.; Cincinnati College of Medicine and Surgery, 1898; died in Portland Sept. 22, aged 83, of cerebral hemorrhage.

Schiltz, Frank A. ✠ Decatur, Ill.; University of Illinois College of Medicine, Chicago, 1951; interned at the Indianapolis General Hospital; formerly chief resident physician at the MacNeal Memorial Hospital in Berwyn; served during World War II; died Nov. 12, aged 33.

Stephens, Virgil Ray ✠ Berwyn, Ill.; Northwestern University Medical School, Chicago, 1914; fellow of the American College of Surgeons; formerly on the faculty of the University of Illinois College of Medicine in Chicago; served on the staff of the West Suburban Hospital in Oak Park, Ill., and the MacNeal Memorial Hospital; died in De Land, Fla., Dec. 2, aged 73.

Sutton, Edward Forrester Holden, Amenia, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1899; died Sept. 10, aged 81, of cerebral vascular accident and arteriosclerosis.

Thabes, John Alois Jr. ✠ Brainerd, Minn.; University of Minnesota Medical School, Minneapolis, 1927; fellow of the American College of Surgeons; on the staff of St. Joseph's Hospital, where he died Oct. 14, aged 54, of cerebral hemorrhage.

Updegraff, Chester Deric, Medicine Lodge, Kan.; College of Physicians and Surgeons, Medical Department of the Kansas City University, Kansas City, Kan., 1903; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; formerly practiced in Greensburg, where he was coroner of Kiowa County; died Oct. 4, aged 74, of a heart attack.

Vander Veer, Frank Leroy ✠ Janesville, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1894; on the staff of the Sartori Memorial Hospital, Cedar Falls; died Oct. 13, aged 86, of coronary heart disease.

Ware, Ford, Macon, Ga.; University of Georgia School of Medicine, Augusta, 1912; member of the Medical Association of Georgia; formerly on the staff of the Macon Hospital; died in the Middle Georgia Hospital Oct. 4, aged 66, of coronary thrombosis.

West, Richard Thomas ✠ Washington, D. C.; George Washington University School of Medicine, Washington, 1905; member of the American Urological Association; life member of the Medical Society of the District of Columbia; consultant in urology at the Garfield Memorial Hospital, where he joined the staff in 1911 as associate in urology and later became visiting urologic surgeon; on the staff of the Doctors Hospital, where he died Sept. 19, aged 83, of bilateral pyelonephritis with cystitis.

Whelchel, Fred Cooper, Rome, Ga.; University of Vermont College of Medicine, Burlington, 1918; member of the Medical Association of Georgia; chief of the x-ray department of the Battey Hospital; died Oct. 23, aged 64, of tracheobronchitis.

Wilson, Hermon Fowler, Menlo Park, Calif.; College of Physicians and Surgeons of San Francisco, 1898; an associate member of the American Medical Association; died in Palo Alto (Calif.) Hospital Nov. 28, aged 81, of cerebrovascular thrombosis and arteriosclerosis.

FOREIGN LETTERS

AUSTRIA

Electric Burns.—At the meeting of the Society of Physicians in Vienna on Nov. 4, Dr. W. Wittels reported on a 27-year-old patient who had accidentally absorbed a 15,000 volt current, thereby incurring burns involving 75% of his body surface. When shock had subsided after the infusion of 16 liters of fluid and rest in a water bed, the necrotic tissue was excised. Within a month after the accident, the first isotransplantation was performed, and the second was performed two weeks later. A total of 16 skin flaps obtained from eight donors was applied. Almost complete take occurred, and thereafter two autotransplantations were performed, but the patient died on the 63rd day of his illness. This report illustrates the fact that a patient may survive a serious electric shock and that isotransplantations may prolong his life but that death cannot be prevented when not enough skin is available for autotransplantation.

Intraossal Phlebography.—At the same meeting, Dr. H. Wild reported experiments in which a contrast medium was introduced into the marrow cavity of long bones of dogs. The results of microscopic examination of various tissues suggested that a contrast medium when injected twice into the bone marrow does not cause serious impairment in an otherwise healthy animal. Repeated injections, however, should not be made at the same spot, since acute inflammatory reactions may occur in the soft tissue. In the bone the normal walling off by connective tissue and callus from the rest of the marrow cavity may be delayed for a long time, and the only result may be the formation of a wide layer of fibrillary marrow. These findings suggest the occurrence of tissue damage. The results of examination of the other organs justify the conclusion that distant impairment may not be expected. There is spontaneous healing, but it takes a long time.

Bronchial Carcinoma.—At the meeting of the Society of Physicians in Vienna on Oct. 21, Dr. G. Salzar reported that, in a series of 1,017 patients with bronchial carcinomas who were treated surgically, 612 of the tumors could be resected and the rest were inoperable. After radical resection, 45% of the 612 patients survived 18 months, and four years later 24% were still alive. Although it is often asserted that patients who have undergone pneumonectomy are pulmonary cripples unable to live a normal life, 25% of these patients were able to work more than four years after their operation. Despite the relatively small number of patients who obtain permanent cure, the favorable results make the surgical treatment of bronchial carcinoma worthwhile.

ENGLAND

Influenza Vaccine Trials.—The Medical Research Council's committee on clinical trials of influenza vaccine has published its second progress report on the use of oil adjuvants with influenza vaccines (*Brit. M. J.* **2:**1229, 1955). Since the previous report it has been found that mouse-adaptation of an influenza virus appears to confer an improved antigenicity on the strain when the latter is compared with the same virus passed through eggs. This suggested a further trial comparing mouse-adapted and egg-adapted virus vaccines made from the same strain but to which oil adjuvants had also been added. The study was designed to test the antibody response to the mouse-adapted line of the Liverpool strain of virus A in both a saline and an emulsified oily medium and the egg strain in an emulsified oily medium only. Inoculations were carried out on 399 volunteers in 11 centers. Blood samples were collected before inoculation and at intervals of two and four weeks and 3, 6, and 12 months after inoculation, and hemagglutination inhibition tests were carried out, with standard antigens and standard pools of human plasma used for control purposes. General and local reactions to the inoculations were also noted. It was found that the emulsified oily vaccines gave a greater and more sustained antibody response than the saline vaccine in spite of the fact that they contained only one-tenth the amount of virus antigen. A decrease in the antibody levels found a year after inoculation occurred in all the vaccinated groups. There was no significant difference in the general reactions produced by any of the vaccines, but the local reactions were more numerous in those given the saline than in those given the oily vaccines. Comparison of the antibody titers obtained with egg-adapted and mouse-adapted virus vaccines was in favor of the latter, but it was thought wise to delay interpreting this observation and to compare the protective value of the two lines of virus. McDonald and Andrews have carried out trials comparing clinical and laboratory tests in the diagnosis of influenza (*Brit. M. J.* **2:**1232, 1955). They concluded from their results that the assessment of a vaccine on purely clinical grounds might understate the degree of protection afforded by a vaccine, whereas one based on serologic findings might exaggerate it. They concluded that, until it is shown that influenza can be detected by serologic methods equally well in persons who have received an influenza vaccine and in those who have not, serologic diagnosis should not be the only method of diagnosis used in a vaccine field trial.

General Practice in Scotland.—In its annual report the Scottish Medical Practices Committee reviews the position of general practice in Scotland up to the end of June. There were then 2,568 physicians providing general medical services under the National Health Service, compared with 2,543 in 1954. The average number of patients on each physician's list at the end of June was 1,975, compared with 1,981 in 1954. There would thus appear to be no shortage of general practitioners. This is supported by the statement that applications for 22 advertised vacancies numbered nearly 900; however, many physicians applied for more than one vacancy, and applications came from physicians already established in practice. The average age of physicians for these vacancies was 39. The main method of entering general practice is to reply to advertised vacancies as an assistant. Setting up a new independent practice with the small grant allowed by the Ministry of Health (about $850 a year) is not very popular. Few young physicians wish to take the risk of building up a new practice from scratch, even in the so-called under-doctored areas. Owing to the housing and office space shortage, there is often difficulty in finding a suitable location. Moreover, if patients are already on the list of a national health service physician, they are not likely to change to a newcomer. Before the National Health Service was introduced, patients were more mobile than they are today, when patients can change their physician only by applying to the executive council. The Scottish Medical Practices Committee considers that the most effective method of getting into general practice is by entering into partnership with another physician after serving a preliminary apprenticeship, but this can be done only with the cooperation of physicians already established, and many do not seem to be sufficiently cooperative.

New Antitumor Agent.—The compound, *p*-(di-2-chloroethylamino)-phenylbutyric acid, (C. B. 1348) has been submitted to clinical trial for the treatment of malignant lymphomas by Dr. D. Galton and his co-workers (*Brit. M. J.* **2:**1172, 1955). The conditions treated were Hodgkin's disease (23), lymphocytic lymphoma (20), reticulum cell sarcoma (11), and giant follicular lymphoma (6). The dosage, by mouth, ranged from 2 to 20 mg. daily. A few patients received the sodium salt intravenously. A course of treatment usually lasted three to six weeks, and several patients received more than one course. Treatment was stopped when satisfactory improvement had been obtained. Prolonged treatment was given when improvement was progressive and the blood findings offered no contraindications. The largest total dose given was 1.93 gm. in the course of 12 months'

The items in these letters are contributed by regular correspondents in the various foreign countries.

continuous treatment. Of 60 patients treated, 20 were sufficiently improved to be able to return to a fairly normal life for at least six months. Improvement of shorter duration was observed in 26. The results were poor in reticulum cell sarcoma, in which condition no patients received any benefit. Of the 23 patients with Hodgkin's disease, 18 received some benefit. The best results were obtained in patients with giant follicular lymphoma, all of whom were benefited. In the less seriously ill patients, outpatient supervision was satisfactory, with weekly hemoglobin determinations, total and differential leukocyte counts, and examination of skin and mucosa for hemorrhagic phenomena. Clinical improvement was usually evident within three weeks of treatment. Galton and his co-workers consider that CB 1348 is less damaging to hematopoietic tissue than the other cytotoxic agents hitherto available for the treatment of malignant lymphomas.

Physician's Obligations.—A suit was brought against a physician in the National Health Service, alleging refusal to treat a patient when she was ill. The plaintiff stated that she suffered from heart disease, lumbago, hypertension, and migraine. When she called at the physician's office on Christmas day claiming treatment, she was told that there was nothing wrong with her and that if she was not satisfied she could go to another physician. She refused to leave and was eventually removed by the police. She alleged that her sufferings in mind and body were increased by the physician's actions and that she was confined to bed afterwards. The judge said that in a case of real, acute emergency a physician under the National Health Service was obliged to treat any patient who was acutely ill, e. g., a person in a road accident or someone in a critical condition. His obligation under the health service was to render all necessary and proper treatment to his patient. To ascertain what treatment was necessary, reasonable skill had to be exercised to make a diagnosis, but in the case of a chronic illness, such as that of the plaintiff, this duty did not mean that the physician was required to make a full clinical examination every time the patient requested it. In this case the physician had seen the patient frequently for about a year. Without hearing the defense, the jury stopped the suit. Judgment was made in favor of the physician with costs.

FRANCE

Irradiated Antirabic Vaccine.—At a meeting of the Academy of Medicine, Hasegawa and his co-workers criticized the classic antirabic vaccination, which may be followed by a delayed Korsakoff psychosis even after 20 years. Using a rabies virus from the Pasteur Institute, the authors have prepared a new vaccine. After 50 intracerebral passages in guinea pigs, the animal's brain is removed and a 10% emulsion is prepared. One cubic centimeter is then placed in a Petri dish and exposed to ultraviolet irradiation for 10 to 30 seconds at a distance of 10 cm., thus assuring inactivation of the virus. After having tried the preparation in mice, the authors have given a daily subcutaneous injection of 1 cc. and an intradermal injection of 0.2 cc. of this vaccine for 15 days. A series of patients bitten by an animal in which rabies virus was found, or in which histological examination of the brain or inoculation of brain emulsion into a mouse revealed rabies, were followed for six months. Of 448 treated by the new vaccine, protection was obtained in 100%. Of 460 treated with the classic vaccine, 20 died. Paralytic accidents were less frequent with the new vaccine (0.06% compared with 0.5%).

Hypothermia.—Monod and Juvenelle in *Journal français de médecine et chirurgie thoraciques* (no. 3, 1955) report a hypothermic technique that abolishes consciousness, induces general anesthesia, and blocks the thermoregulating centers. Infants and children are immersed in ice water, and ice bags are applied over the body surface in adults. No shivering is observed, and the body temperature drops to 77 F (25 C) within five hours. No discomfort is noted with the lowering of temperature, but the rewarming is a delicate process and not without danger. This method of hypothermia has permitted surgeons to perform long operations for congenital cardiac malformations in babies and children, operations requiring artificial cardiopulmonary circulation, and operations whenever an anoxia is feared.

Controlled Hepatectomy.—In performing partial hepatectomy the normal blood supply of the different portions of the liver must be preserved. In *Gazette médicale de France* (no. 61, 1954, pp. 1991-1998) Lortat Jacob reports that controlled hepatectomy is indicated in the excision of a hepatic tumor that has metastasized by contiguity, as that of the ascending colon, and when a total excision of the tumor and the contiguous normal tissue is required. In patients with hemangioma, lymphangioma, solitary adenoma, or cystic cholangioma, this method would be preferred to partial resection, which may prove dangerous because of the large blood vessels in the vicinity. In patients with certain liver traumatisms or hydatid cysts, a controlled lobectomy assures hemostasis without danger of liver hemorrhage.

New Hypotensive Agents.—At a meeting of the Academy of Sciences in March, Raymand Hamet reported that Hunteria eburnea pichon, an African apocynaceous plant, has actions similar to those of Rauwolfia serpentina and Rauwolfia heterophylla but more prolonged and not accompanied by any reduction of cardiac activity. It possesses a sympatheticosthenic action. Dr. Dang-Van-Ho of Vietnam reported good results with an extract of Morinda citrifolia root, a rubiaceous plant found in Saigon.

ITALY

Congress of Stomatology.—At the 30th Italian Congress of Stomatology in Naples in September, Professor Armenio of Bari described his operation for trigeminal neuralgia, which is common in the aged. The advantage of his method, which consists of operating on the peripheral branches of the nerve, lies in the fact that only delayed regeneration of the fibers interrupted by the nerve resection occurs. Because of this feature, the method is preferred for the aged to an injection of alcohol into the gasserian ganglion or a retrogasserian neurotomy, both of which are more difficult and more traumatic. Prof. Beniamino De Vecchis of Rome said that prognathism affects the mortality rate of infants because it reduces the quantity of oxygen reaching the lungs. This condition should be corrected early by mechanical means and respiratory reeducation to increase the vital capacity. Early correction can be accomplished because, up to the 12th year of life, the bones of the face are still flexible and pliable. Correction at a later age requires the extraction of teeth on both sides in order to push backward the protruding maxillary segment.

Professor Mancini of Rome reported on nutrition as it relates to dental caries. In the prenatal period dietary deficiencies, if prolonged and marked, can affect the teeth of the fetus. In the presence of vitamin A deficiency, the differentiation of the ameloblasts does not take place in the normal manner and the adjacent mesenchymal tissue will form atypical dentin. Disturbances of calcification may take place because of a specific deficiency of calcium or of trace elements. Likewise, in the postnatal period, general or specific deficiencies in the diet may influence the process of calcification, with hypoplasia and hypocalcification of the enamel. Vitamin C can influence favorably the collagen tissue and the intercellular substances, and it can also modify the structure of the odontoblasts, dentin, pulp, and enamel. Calcium and phosphorus are brought to the tissues of the tooth through the vascular reticulum of the pulp and are deposited there at first by means of a phosphatase. A calcium-phosphorus imbalance may cause disturbances of calcification. Although its mechanism of action is still undetermined, vitamin D plays a part in the process of calcification. The influence of a deficiency of proteins or indispensable amino acids on the normal structure of the tooth is still undetermined.

Vitamin E.—At the third International Convention on Vitamin E in Venice in September, it was agreed that vitamin E is one of the most indispensable of vitamins. When it is entirely withdrawn from the diet, muscular dystrophy, impairment of reproductive power, atherosclerosis, and diabetes mellitus may develop in laboratory animals. When the vitamin is restored to the diet, the animals recover. Similar results have not been

demonstrated in man. Although vitamin E is no doubt necessary also in man for the protection of vascular integrity, glandular secretion, and elasticity of the muscles, its deficiency in man is immediately counterbalanced in a manner not yet understood. Despite the fact that laboratory animals that have been rendered arteriosclerotic, diabetic, or myopathic are definitely benefited by the administration of vitamin E, persons having the same diseases do not react in the same way to this vitamin. Unlike Dr. Evans Shute of Montreal, Canada, who reported brilliant clinical results in the treatment of wounds and burns with large doses of vitamin E, Professor Vannotti of Lausanne, Switzerland, was less optimistic about the therapeutic action of vitamin E in man.

PERU

Effect of Diuretics in Cirrhotic Patients.—In an address before the second Peruvian Congress of Medicine in October, Dr. Kehl Markley, United States Public Health Service, working in the Instituto de Biologia Andina, said that some factor or factors in the cirrhotic patient prevent the normal excretion of the kidneys. Such phenomena increase as the disease progresses, possibly due to hormonal agents. Apparently these factors do not have much effect on the action of mercurial diuretics. The speaker investigated the effect of diuretics in 24 cirrhotic patients between the ages of 24 and 74 years. All of them had some degree of ascites and required frequent paracenteses. Diseases other than cirrhosis that produce ascites were ruled out. Many of the patients had reached an advanced stage of the disease, since eight of them died after completion of the study. A definite diagnosis by liver biopsy or by direct visualization of the liver at autopsy was made in 10 of them. In the trial, Esidrone, potassium chloride, and acetazolamide were given to each patient, and throughout the study the intake of liquids and foods remained constant. The administration of each diuretic was preceded by a two-day control period, in order to rule out the influence of one drug on another. Acetazolamide was given in doses of 250 mg. twice daily; 8 gm. of potassium chloride dissolved in a syrup and colloidal solution was given orally in divided dosage for a period of two days; and 2 cc. of Esidrone was injected intramuscularly on one day only. No adjunctive therapy was given except for the administration of vitamins. Urine was carefully collected daily, measured, and analyzed for sodium and potassium ions in the flame photometer and for chloride ions by the method of Hiller and Van Slyke. Patients were weighed daily. The results showed that the daily urinary excretions of water, sodium, potassium, and chloride during the administration of acetazolamide and potassium chloride diminished progressively as the disease increased in severity, while the total daily excretion of the same elements did not notably vary with the use of Esidrone. The loss of weight after the use of acetazolamide and potassium chloride also diminished with the progression of the disease, whereas, during the administration of Esidrone, the loss of weight was not affected by the severity of the condition. From a practical standpoint, therefore, Esidrone is the diuretic of choice.

Award for Research in Bartonellosis.—The Alberto Barton award annually granted for the best Peruvian research in the field of bartonellosis was given in October to Dr. Pedro Weiss, professor of pathology at the School of Medicine. He discovered that contracting the acute form of the disease depended not only on infection with Bartonella bacilliformis but also on a lowering of the immunity that is difficult to observe in most of the natives living in endemic regions, who usually suffer from the benign form characterized by a warty eruption. Dr. Weiss showed that patients who died of bartonellosis generally did so at the beginning of the remission and not, as was believed, during the acute phase, in which the anemia and impairment of general health reaches its peak. He also showed that during the acute phase a specific immunity develops while the nonspecific resistance decreases. These observations led to the belief that intercurrent infections arising during the acute phase were the cause of death in most cases. This has been now confirmed by several investigators, who have found salmonellosis to be the most frequent intercurrent infection.

Acclimatization.—Prof. Carlos Monge in *Anales de la Facultad de medicina* (vol. 38, no. 1, 1955) states that acclimatization can be congenital or acquired. The physiological and biochemical systems of the human body differ at distinct altitudes, but their homeostatic integration is always necessary for stability. Any climate change stimulates adaptive processes. The population living at sea level and capable of living at higher altitudes can be represented by a trapezium, in which the superior base shortens as the altitude increases. There are persons who cannot adapt themselves to a given altitude, although they can live normally at altitudes 1,000 to 3,000 ft. (304.8 to 914.4 m.) above sea level. Chronic mountain sickness in its clinical or subclinical form eliminates those who cannot become acclimatized, by virtue of the fact that, even when they feel well at the higher altitude, they cannot reproduce. Fertility is, therefore, an index of the real degree of acclimatization achieved. It is not clear, however, whether only reversible adaptive mechanisms are involved or whether there are underlying genetic factors.

Pyridoxine in Anesthesia.—Ambulatory patients with fractures generally show unpleasant postanesthetic symptoms that prolong their stay in the hospital and require the attention of hospital personnel. To remedy this, Drs. Renzo Corno and Carlos Deza gave pyridoxine chlorhydrate for such postanesthetic symptoms (*Boletin del Colegio de investigaciones medicas*, vol. 1, no. 1). The trial was carried out in 20 unselected patients with fractures, whose ages varied from 4 to 60 years. A similar group of 20 patients served as a control. General anesthesia with trichloroethylene was used in all cases. Of the pyridoxine-treated patients, 17 had no postanesthetic symptoms, but all of the patients in the control group showed some degree of intolerance to the anesthetic. Pyridoxine was particularly helpful in preventing such symptoms as nausea, vomiting, protracted drowsiness, and sweating. The authors recommended giving the drug intravenously at the beginning and end of the anesthesia in doses of 100 mg. for adults or 50 mg. for infants in 10 cc. of sodium chloride solution.

SWEDEN

Nobel Prize Winner, Professor Theorell.—The 1955 award of the Nobel prize in physiology and medicine to Professor Nils Hugo Theorell of the Nobel Institute in Stockholm was greatly appreciated in Sweden, which enjoyed this distinction also in 1911. Theorell was born in 1903. He obtained his medical education in Stockholm, qualifying in medicine in 1924 and being awarded the degree of doctor of medicine in 1930. In 1935 he was awarded a Rockefeller scholarship, and he spent three years with another Nobel prize winner, Otto Warburg, at the Kaiser Wilhelm Institute in Berlin. It was here that some of his most important work on the fission of enzymes was done. He has also been associate professor of medical chemistry at the University of Uppsala. Since the creation of the biochemical department of the Nobel Institute in 1937, he has been in charge of its experimental work. While his work on enzymes is fairly well known, little has hitherto been known of his recent work on the combustion of alcohol in the body and on a method for determining the alcohol content of the body.

Mass Radiographic Examination of the Chest.—In the period 1950 to 1954 more than a million persons were screened by mass radiography of the chest. In the *Quarterly Journal of the Swedish National Association Against Tuberculosis* (vol. 50, no. 3, 1955) Dr. Sylve Wijkström reports that hitherto unknown cases of tuberculosis were discovered in 1.6 per 1,000 persons so examined. Most of these were in persons between the ages of 30 and 60 years, and 206 of them had cavitation or positive sputum. In addition to these new cases of tuberculosis, which in themselves fully justified the system of mass radiography, 422 patients with Boeck's sarcoid were found, 362 of whom had not previously been diagnosed. Intrathoracic tumors, chiefly lung cancer, were found in 339 patients, or 0.32 per 1,000 examined. Cardiovascular diseases were discovered in 2.9 and silicosis in 0.37 per 1,000 examined. Altogether 12,504 persons, or 11.7 per 1,000, were found to have significant lesions.

CORRESPONDENCE

EXPLOSION HAZARD DURING ANESTHESIA

To the Editor:—During transurethral surgery performed under thiopental (Pentothal) sodium–nitrous oxide–curare anesthesia, the anesthesiologist noticed a sparking sound accompanying each electrical manipulation, the smell of burning rubber, and the appearance of smoke. A few moments later, sparks were seen to pass from the operating table to one of the breathing tubes, where it lay across the painted metal edge of the table; the rubber breathing tube was later found to have been burned but not perforated. The anesthesia machine was immediately pushed away from the operating table and the anesthesia system converted from thiopental–nitrous oxide to thiopental–air. It was quickly found that the wire grounding the operating table was not making proper metallic contact with the ground pipe. The electric charge on the table therefore mounted, and finding intermittent contact with the conductive rubber breathing tube, the anesthesia machine and the tube became converted into a sort of ground; continuous and sparking current flowed from the edge of the table to the conductive rubber tube (and into the anesthesia machine), producing a large amount of heat. Had the tube been perforated, the combination of sparks and oxygen might have exploded any inflammable material nearby, as the rubber tube itself. In considering the danger of explosion, two kinds of electricity must be considered: the ordinary kind that is supplied by house current and batteries, and the static form that originates anywhere and commonly occurs on the surfaces of nonconductors. This country, with its dry atmosphere, has come to fear the static type more than, and too often to the exclusion of, current supplied by electrical wiring. Where the static danger is not great, as during thiopental-nitrous oxide anesthesia, and where the electrical wiring hazard is high, as in transurethral surgery, it is suggested that the customary policy concerning operating room explosions be reversed where it applies to the electrical intercoupling of the operating table and the anesthesia machine, and that conductive rubber breathing tubes not be used, as they invite the danger of grounding the operating table in a hazardous manner and fail to prevent and may actually cause an explosion.

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INTERNATIONAL MEDICAL ORGANIZATIONS

To the Editor:—The recent reports in THE JOURNAL on the activities and potentialities of the World Medical Association prompted me to add a statement concerning the importance to physicians in the United States of the program of the Council of International Organizations in the Medical Sciences. It should be noted that the World Medical Association is a member of the council and that their interests are common ones. The council is an international interdisciplinary organization formed to promote cooperation of voluntary nongovernmental international organizations in the various branches of medicine. Its main interests have been in assisting in the planning for international congresses, in organizing scientific symposiums, in arranging conferences to assist international collaboration in making medical literature more accessible, and in working on similar projects. In general, the council is operating to improve and facilitate "communication," both oral and printed, among students of all branches in medicine, in all parts of the world. Its uniqueness lies in the fact that it is the only organization that embraces the entire field of medicine and clinical and fundamental sciences, through the membership in it of the major international organizations in each field. The council is supported in part by the World Health Organization (WHO) and by United Nations Educational, Scientific and Cultural Organization (UNESCO), because it can perform important functions that those intergovernmental agencies cannot do directly. At the present time the council is expanding its program and is looking for private support from persons or foundations having an interest in the promotion of human welfare by assisting in international cooperation in promoting medical science and its applications. This private support will be in addition to WHO and UNESCO subsidy. Mr. Paul van Zeeland of Belgium is the chairman of an international committee seeking such support. He will be aided by interested persons in many countries, and assistance from United States physicians in stimulating interest will be much appreciated and, in fact, is needed.

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DIABETIC RENAL COMPLICATIONS

To the Editor:—Diabetic renal complications of the intercapillary glomerulosclerosis (Wilson-Kimmelstiel) type are commonly seen at a stage where neither control of sugar or salt, drugs, or other known treatments avail to stop the progression to fatal uremia. The markedly increasing mortality and the generally gloomy prognosis were my reasons for the report of a single case (*Arch. Pediat.* **72:**250 [Aug.] 1955). In 1922, when the patient was 6 years old, his severe diabetes was controlled in the Physiatric Institute, first with undernutrition and later with insulin. Later he managed his own treatment with symptomatic success, so that he grew up normally and never missed a day from work. For some 15 years back, there were occasional observations of slight albuminuria, hypertension, and tachycardia. After the symptoms increased, he was hospitalized in November, 1954, and returned to me because of an imminently fatal prognosis. He had uremic malaise, vomiting, nosebleeds, edema, albuminuria with gravity fixed at 1.010, blood pressure 210/110 mm. Hg, pulse rate of 120 per minute at rest, angina requiring phenobarbital and about 20 glyceryl trinitrate (Nitroglycerine) tablets daily, anemia of 2,800,000 red blood cells per cubic millimeter, normal leukocyte count, blood-urea-nitrogen level of 215 mg. per 100 cc., creatinine of 15 mg. per 100 cc., and basal metabolism of +2. Remarkably, the vision was perfect and the eye grounds were normal. Any trifle of salt aggravated edema, hypertension, and angina, while saltless diet caused intolerable muscle pains and increased uremic symptoms. Such a degree of renal insufficiency is a recognized contraindication to adrenal or hypophysial operations. Furthermore, practical reasons necessitated treatment at home, with dependence on the patient's dietary training and analyses from a commercial laboratory. After routine emergency measures, the main attempt to spare the renal function consisted in reducing not merely the protein metabolism, as has been done heretofore, but also the protein mass of the body and keeping it reduced. This concept of relations between body mass and organ load is an adaptation of a principle of diabetic diet. The application in this instance consisted in two months of practically protein-free diet and a 15-gm. protein diet for seven weeks thereafter, with liberal carbohydrate and fat calories. During this time, saltless diet became tolerated and edema and angina ceased. The blood-urea-nitrogen level fell gradually to 50 mg. per 100 cc. and the creatinine to 7.6 mg. per 100 cc. The patient became subjectively normal except for weakness. The prolonged negative nitrogen balance changed to equilibrium on a diet of 30 gm., later on 20 or 25 gm., of protein daily. The patient resumed his regular work as a salesman, continuing for almost one year. The continued control of blood nitrogen, hypertension, and subjective symptoms conformed to theory. Anemia was unchanged. The one favorable feature at the beginning had been the absence of severe electrolyte disturbance, and the lack of adequate precautions on this point was the mistake that resulted in rather acute death. It is hoped to employ some new methods for this purpose in future cases and thus perhaps to improve further the prognosis of this condition.

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BUSINESS PRACTICE

THE DOCTOR LOOKS AT MUNICIPAL BONDS

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Because a doctor's work is intensely personal, not only in respect to his relationship with his patients but also as regards his undivided, frequently unshared, individual responsibility in connection with each case, it follows that a doctor's investment program should be built around securities that provide the combined advantageous features of maximum safety and minimum care and supervision as well as the most favorable effective net returns.

A doctor's practice requires a reliance on himself that is absolute and inescapable to a degree probably not even approximated by men engaged in business or industry. It may be said that a doctor is probably more dependent upon his individual efforts, his individual decisions, and his success at keeping individually fit and able than men in other professions or occupations. For this reason a doctor's investments should be of a type that will take the least toll of worry and care—and taxes.

High-grade state and municipal bonds satisfy the requirements that could be considered essential for a doctor's investments to a greater extent probably than any other type of security. Ranking in quality second only to obligations of the United States Government, prime state and municipal obligations are based on the full faith and credit and taxing power of sovereign states and substantial communities. Municipal bonds provide the most impregnable credit standing of any type of security excepting only the obligations of the federal treasury. To illustrate the success with which municipal bonds have met the challenge of economic catastrophe, it may be pointed out that at the depth of the devastating depression of the 1930's less than 2% of the state and municipal bonds then outstanding were in default. Virtually all of the situations comprising even that miniscule percentage of defaults were cured and paid out over a reasonable period of time.

Granting that the medical profession requires complete dedication, it may be in point to observe that state and municipal bonds, which are less subject to the vagaries of day-to-day developments, marketwise as well as otherwise, than any other class of securities, appear to be especially appropriate for a doctor's investment portfolio. From the standpoint of intrinsic security, the obligation of a strongly situated state or a conservatively managed municipality enjoys stability not found in the corporate obligations of commercial enterprises whose affairs and prospects may tend in natural course to fluctuate constantly and widely. For this reason, a municipal bond portfolio requires less time in actual review and supervision than one including other types of securities. Only the shift of interest rates affects the longer term price changes in carefully chosen state and municipal bonds.

Furthermore, again from the standpoint of detail, state and municipal bonds possess a unique advantage over other securities because the interest paid thereon is fully exempt from federal income taxes under present laws, decisions, and practice. Not only is no federal income tax liability involved, but also the interest received on state and municipal bonds need not even be reported on the federal income tax information return. To a hard-pressed doctor, eager to minimize as much as is prudent the time spent on his investment account, the simplicity of handling municipal bonds cannot be other than overwhelmingly appealing.

That the advantage of the "tax-exempt" feature of state and municipal bonds is not confined to the area of convenience alone becomes dramatically apparent when the full benefit of tax exemption is understood. From widely available tables prepared for ready reference, examples involving valid comparisons of tax-exempt yields with their taxable counterparts strikingly reveal the advantages accruing to the tax-free income on municipals. The refuge thus afforded is being sought by a constantly increasing number of members of the medical profession, in which substantial incomes are so frequently encountered.

To the features that should make state and municipal bonds peculiarly appropriate for a doctor's investment account, to which reference has been made above, there is a further addition. Municipals are traditionally issued in serial maturities; that is, they are put out with a selected portion of each aggregate issue maturing or being paid off annually over a given period of years. An investor, therefore, is able to arrange a "maturity schedule" or pattern of maturing bonds so he can plan precisely and confidently on when certain amounts of money that have been invested in municipal bonds will be returned to him. For doctors who do not have access to adequate pension plans, which have gained such wide acceptance in business and industry, and who make up for their lack by a carefully worked out saving program, the systematic tailoring of an investment account that will make funds available year-by-year over some stipulated period in the future strongly suggests the use of municipal bonds. Their serial set-ups, which permit selection of bonds maturing in any desired year or years, make municipals an outstandingly convenient if not an essential ingredient of such an investment program.

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MEDICAL FILM REVIEWS

Too Young to Say: 16 mm., color, sound, showing time 13 minutes. Produced in 1955 by the Cinema Department of the University of Southern California by William Mehring in cooperation with the John Tracy Clinic, Los Angeles. Sponsored by the Beltone Hearing Aid Company, Chicago. Procurable on loan from Harshe Rotman, Inc., 8 S. Dearborn St., Chicago 3.

This film explains how the John Tracy Clinic has made the measurement of hearing into a game for small children. The effect of this game is to tell the operator when the child is hearing "beeps" emitted through an audiometer. An adult generally will indicate that he has heard by raising a hand; however, it is almost impossible for a 2 or 3-year-old to understand this procedure. The first step is to have the child play the game by assembling part of a simple toy each time he hears the beat of a drum. Gradually, the transition is made from drum beat to audiometer "beep" and earphones. This film is interesting from beginning to end and shows the difficulties and possibilities of audiometric testing in children down to the age of about 18 months. It is recommended for pediatricians, medical students, and PTA groups. As a production, it is well done. It is well organized, and the color quality and narration are good.

The Invader: 16 mm., black and white, sound, showing time 37 minutes. Produced in 1955 by the Center for Mass Communication of Columbia University Press under the auspices of the Georgia Department of Public Health, with the guidance of Charles Daniel Bowdoin, M.D. Procurable on rental ($8) or purchase ($135) from Center for Mass Communication, 1125 Amsterdam Ave., New York 25.

The purpose of this film is to make the general public aware of the dangers of syphilis. It traces man's efforts since the 15th century to cope with a baffling and dismaying problem and shows the step-by-step development of medical knowledge and the changes in public attitude toward the disease. The film tells its story through the available documents of each age. The story from the 15th to the 19th centuries is dramatized by means of contemporary woodcuts, engravings, paintings, and drawings by such artists as Dürer, Breughel, Hogarth, and Daumier. The later story is enriched with historical photographs of such pioneers as Ehrlich and Hata and motion picture records of the work of Fleming, Mahoney, and others. This is a compelling film that will be useful for social studies classes, health education, and in some cases for students in the medical professions. It could also be used in clinic waiting rooms. Its production techniques are unusual, and, combined with the well-told story, they will hold the interest of such audiences. As a teaching device, it is beautifully done.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Observations on the Mechanism of Intranasal Absorption of Vitamin B_{12} in Pernicious Anemia. R. W. Monto and J. W. Rebuck. Blood **10:**1151-1155 (Nov.) 1955 [New York].

The authors cite some of their earlier reports on the nasal instillation of vitamin B_{12} in pernicious anemia, pointing out that in the past three years 32 patients with pernicious anemia in relapse and 55 in remission have been controlled satisfactorily by the intranasal administration of vitamin B_{12} either in a saline solution or lactose powder or as crystals. In this paper they are concerned chiefly with the mechanism of absorption of vitamin B_{12} by the nasal mucosa. Satisfactory clinical and hematological response was obtained from the single application to the nasal mucosa of 200 and 150 mcg. of crystalline vitamin B_{12} in two patients with pernicious anemia. Absorption of the vitamin was probably direct and did not require binding with "intrinsic substance." Chronic disease of the nose did not contraindicate this mode of therapy; local irritation of the mucous membranes by the crystalline B_{12} or the vehicle employed has not been observed.

Return to Neurothyroid Concept of Basedow's Disease. H.-P. Klotz and P. Lumbroso. Semaine hôp. Paris **31:**3430-3433 (Nov. 6) 1955 (In French) [Paris, France].

Recent theories concerning thyrotoxicosis hold that the disorder is due to hypersecretion of the thyroid-stimulating hormone by the hypophysis. A number of facts are presented showing that this is not the case in a majority of patients. The authors lump together all those clinical forms that are characterized by tachycardia, tremor, emaciation, and elevated basal metabolism, regardless of whether there is goiter, exophthalmos, or diffuse or nodular hyperplasia of the gland. The rationale for considering these symptoms as one entity is that they all respond to a common therapy. The disease is caused by a particular state of both the thyroid gland and the nervous system, which can occur only in patients having a double predisposition to it. It is the manifestation of a state of imbalance between nervous system receptors and thyroxin secretion, that is, there is disturbance of the cerebral cortex and the vagosympathetic system caused by a secretion of thyroxin too strong for these receptors. Either one of the two poles, nervous or thyroid, may be at the base of the disequilibrium, but they are always interrelated. The authors explain both the psychosomatic and the postmenopausal or postcastrational forms of thyrotoxicosis on the basis of their concept. Both curative and preventive therapy must be directed toward the two factors involved. Nothing can be expected from pituitary-inhibiting measures.

Pulmonary Coin Lesions. C. G. McEachern, J. E. Arata and R. E. Sullivan. J. Indiana M. A. **48:**1285-1289 (Nov.) 1955 [Indianapolis].

The term coin lesion has been applied to any spherical pulmonary lesion visible on the chest film surrounded by normal lung tissue and without evident cavitation. Some authors do not include calcified lesions; others include them. Coin lesions vary in size and in the past were frequently diagnosed as "tuberculomas." The absence of symptoms is readily explainable by the location of the lesions. For a lesion to cause cough, it must cause irritation of the bronchial mucosa. Since coin lesions are peripherally placed, they do not impinge on the most sensitive bronchial mucosa. They do not generally cause hemoptysis, atelectasis, or pneumonitis with fever. Bronchoscopy and cytological studies are usually of no value in coin lesions. Skin sensitivity tests for the common fungi, including Histoplasma capsulatum, may be positive but cannot be absolute assurance against malignancy. Calcification is usually evidence against primary malignancy but may be difficult to prove. If one cannot arrive at a definite diagnosis by means of laboratory and x-ray studies and the patient can tolerate surgery, exploratory thoracotomy should be undertaken, for, should the lesion be malignant, the problem may be insoluble when the lapse of time has proved the diagnosis. The risk of exploratory thoracotomy is no greater than that of exploratory laparotomy. The incidence of malignancy in solitary intrathoracic lesions has been reported to vary from 15% to as high as 50%.

Late Results of Isoniazid Intracavitary Treatment. R. Racine and M. Mello Aguerre. Hoja tisiol. **15:**239-246 (Sept.) 1955 (In Spanish) [Montevideo, Uruguay].

Isoniazid intracavitary instillation, given by transparietal puncture, is indicated as a preparatory stage for surgical collapse or for exeresis in treatment of tuberculous cavities after failure of antibiotics given by mouth or failure of artificial pneumothorax. Generally, the cavities are very large, single or multiple, and frequently bilateral. Isoniazid intracavitary instillation often results in complete healing of the cavities, which makes the operation unnecessary. The authors report three cases. The patients were in a very grave general condition. The large unilateral or bilateral cavities in the upper third of the lung did not respond to any of the classical treatments. Isoniazid was given in daily doses of 400 mg. for 17 days to a patient coincidently with, and followed by, administration of the drug orally in daily doses of 200 mg. for three months. The other two patients received isoniazid in doses of 200 or 300 mg. every other day up to a total number of 30 or 57 instillations, also coincidently with, and followed by, administration of isoniazid by mouth in doses of 200 mg. every other day for five months. In all cases the cavities closed entirely by the end of the intracavitary treatment and followed a progressive process of healing with complete disappearance of the cavities in the roentgenograms of the chest within three to five months. Cough and expectoration greatly diminished or disappeared as early as within two weeks in the course of intracavitary treatment, with normalization of the sedimentation of the erythrocytes and reversal of sputum. The patients are clinically cured, as shown by follow-up clinical and roentgen observations, for one, two, and three years, respectively, with bacteriological and tomographic studies. The authors direct attention to the fact that the technique of isoniazid intracavitary instillation by the transparietal puncture is simple and the results are excellent.

Transitory Hepatic Coma: I. Clinical Study. J. P. Benhamou, L. Hartmann and R. Fauvert. Presse méd. **63:**1451-1454 (Oct. 29) 1955 (In French) [Paris, France].

Many clinicians think that hepatic coma represents the terminal stage of liver cell failure and is always fatal. This is not the case, since regression of the coma does occur, either in response to therapy or spontaneously. The histories of four patients with alcoholic cirrhosis are presented; they all had episodes of transient hepatic coma followed at a later date by death from irreversible hepatic coma. Though most often seen in alcoholic cirrhosis of the liver, transitory hepatic coma occurs also in cirrhosis of other causes and, more rarely, in acute hepatitis. Its symptomatology can be divided into two periods: the precomatose and the comatose. The first period is characterized by three types of disturbances, which usually follow each other in this

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The place of publication of the periodicals appears in brackets preceding each abstract.

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order: neurological, behavioral, and orientational. The patient is often unable to remember that he has lost consciousness. The period of coma may be absent altogether; occasionally it occurs unpreceded by the precomatose syndrome, but most often it follows in a gradual manner. It is marked by deep sleep similar to physiological sleep, muscular rigidity, exaggeration of bone and tendon reflexes, occasionally convulsive attacks, and often fetor hepaticus. The coma lasts from a few hours to several days and often disappears abruptly, that is, within an hour. Two factors speak for the transitory nature of a hepatic coma: subtotal loss of consciousness and the presence of a direct provocation. The electroencephalographic disturbances occurring in hepatic coma are described; they are not specific, but strongly suggestive, and are of value for the prognosis.

Alcoholism and Gastric Ulcer. L. Navratil and R. Wenger. München. med. Wchnschr. **97:**1457-1459 (Nov. 4) 1955 (In German) [Munich, Germany].

This investigation was brought about by the observation that the history of many chronic alcoholics revealed an operation on the stomach. Of 200 male alcoholics who were admitted to an institution for mental diseases because of sequels of addiction to alcohol, 19% had earlier undergone gastric resection because of gastric or duodenal ulcer. In an additional 5.5% of these men, the history revealed that a gastric or duodenal ulcer had been demonstrated roentgenologically. Thus about a fourth of the chronic alcoholics had a history of peptic ulcer. The first ulcer symptoms had appeared in many of these men years before they became alcoholics. In several patients periods of gastric complaints and periods of excessive drinking alternated. The authors present case histories that illustrate that a common psychodynamic factor plays a part in the etiology of the alcoholism and the peptic ulcer.

Artificial Hibernation and Inflammatory Processes. F. Purpura and M. Vaccaro. Minerva chir. **10:**866-867 (Sept. 15) 1955 (In Italian) [Turin, Italy].

The results of experimental studies on the onset and evolution of infections in relation to artificial hibernation are reported. Infection was produced in rabbits by injecting intramuscularly a highly virulent broth culture of staphylococci and 1 cc. of a coagulant into the thigh of the animal. Rabbits of the first group received no treatment before or after the inoculation. Those of group 2 were subjected to artificial hibernation after pus had formed at the site of the inoculation. Those of group 3 were subjected to artificial hibernation and inoculated concurrently. Those of group 4 were given 400,000 Oxford units of penicillin daily in two divided doses for five days after pus had formed. Those of group 5 were inoculated, subjected to artificial hibernation after pus had formed, and given penicillin in the same way as those of the previous group. All the animals were killed 10 days after the inoculation. The clinical and pathological evolution of the process was the same in the rabbits that were subjected to artificial hibernation either before or after the inoculation. Local diffusion of the inflammatory process to a stage of frank purulent myositis with secondary degeneration of the adjacent muscle fibers was present in these animals. Signs of connective tissue reaction were not observed. A slight sign of connective tissue proliferation toward the periphery was seen instead in the rabbits that had received penicillin after the induction of artificial hibernation. In the animals in which artificial hibernation had not been induced, the inflammatory process was surrounded by connective tissue proliferation. This was even more marked in the animals that had received penicillin treatment only. The results thus indicated that artificial hibernation, by lowering the tissues' metabolic activity and causing ischemia, decreases the tissues' response to bacterial invasion, and suppurative processes thus have a tendency to diffuse. The authors emphasize that this is due only to inability of the tissues to cope with the bacterial action, because earlier studies had indicated that the bactericidal, opsonic, hemolytic, and lysozymic powers of the organism are modified only very slightly during artificial hibernation. The efficacy of artificial hibernation on septicemia observed by some authors is ascribed to a nonspecific antishock action of artificial hibernation.

A New Synthetic Glucocorticoid: Orientation by Clinical Survey. H. Küchmeister, L. Weissbecker and K. Heinrich. Klin. Wchnschr. **33:**978-985 (Nov. 1) 1955 (In German) [Berlin, Germany].

Prednisone (Decortin) was given to 37 patients, 11 of whom had chronic rheumatic disease, 2 rheumatic fever, 6 adrenal cortical hypofunction (Addison's disease), 2 insufficiency of anterior lobe of the hypophysis, 2 adrenogenital syndrome, 3 lymphocytic leukemia, 5 bronchial asthma, one lymphogranulomatosis, one carcinoma of the liver, one anorexia associated with endogenous depression, one panmyelopathy associated with paramyeloblastic leukosis, and 2 rheumatic carditis. The ratio of the effects of prednisone to cortisone of 1 to 4 to 5 seems to be a suitable basis for the dosage. An initial test dose of 40 mg. of prednisone daily for two to three days is recommended; treatment should be started with 10 mg. and the remaining 30 mg. should be given in divided doses. A subjective and partly objective satisfactory effect became manifest after 24 hours in the rheumatic patients. The maintenance dose lies between 10 and 20 mg. daily and should be reached gradually by reducing the dose of 40 mg. by 5 mg. daily or every second day. With this maintenance dose undesirable side-effects did not occur even when the drug was given continuously for three months. A special diet, poor in sodium and fluids and rich in potassium and proteins, does not seem to be required. Treatment with prednisone should not be abruptly discontinued in order to prevent a relative adrenal cortex insufficiency. For the last three days of prednisone therapy, 20 to 30 international units of repository corticotropin (ACTH) should be given daily, and corticotropin administration should be continued for three to five additional days in decreasing doses. Results obtained suggest that prednisone does not effect a cure but causes improvement of symptoms. It is primarily indicated in patients with rheumatic polyarthritis, and in these patients it is four to five times more effective than cortisone. The substitution effect of prednisone exceeds that of cortisone in patients with adrenal cortical hypofunction (Addison's disease), with insufficiency of the anterior lobe of the hypophysis, and particularly in those with adrenogenital syndrome. Results varied in the patients with bronchial asthma, one of whom became free of complaints after the administration of 50 mg. on the first day and 30 mg. daily for three days; one was free of complaints after he had been given 20 mg. of the drug, while the other three patients were therapeutic failures. Cortisone should be preferred to prednisone for the treatment of patients with lymphocytic leukosis and leukotic panmyelopathy. Cortisone and prednisone in a dose ratio of 1 to 5 proved equally effective in patients with Hodgkin's disease. Prednisone does not seem to be reliable in patients with rheumatic carditis.

SURGERY

Recurrent Carotid Body Tumor: Report of a Case. V. M. Arean. A. M. A. Arch. Path. **60:**530-534 (Nov.) 1955 [Chicago].

Radical excision of carotid body tumors carries a mortality rate of 30%, and, since in most cases these tumors are probably benign, it should not be attempted. Injury to the carotid artery, which cannot always be avoided, usually leads to an ascending thrombosis with the inevitable sequela of permanent hemiplegia or of death following cerebral infarction. Incomplete removal, on the other hand, is certain to be followed by recurrence, as in the case of a 68-year-old man first admitted to the San Juan City Hospital in 1948, in whom local recurrence occurred twice in seven years. The tumor, originally noted two years earlier as a small swelling, had grown slowly until about four months before admission, when it began to increase rapidly in size. Pain and tenderness were not present and the patient had had no difficulty in swallowing. Excision was carried out under ether anesthesia. The surgeon thought he was dealing with an aberrant thyroid and noted that the tumor, which was the size of an orange, was friable and bled easily. The patient, who did well after the operation, failed to report for follow-up and was not seen again until two years later. He was then found to have a mass about 8 cm. across at the site of the previous operation. Removal on

this occasion was incomplete, because the tumor had invaded the surrounding muscles, eroding through the cervical spine at the level of C4 and C5. The patient, however, recovered rapidly as before and was discharged seven days after the operation. Microscopic examination of the specimen showed that the tumor was composed of groups of polyhedral cells with round or ovoid nuclei, finely granular chromatin, and a sharply defined nuclear membrane, separated from one another by bands of connective tissue. Pleomorphism, giant cells, and mitotic figures were not visible. Review of the tissues removed at the first operation showed essentially the same appearance. The third and final operation, at which a mass measuring 10 cm. in diameter was removed, was performed in December, 1953. The tumor had extended into the spinal canal, so that a radical resection could not be attempted; even so, the operation was laborious because of adhesions and excessive bleeding. It went on for five hours and the patient left the operating room in critical condition. He was apparently recovering when, on the seventh postoperative day, he became stuporous and died. Microscopic examination of the specimen removed at the third operation showed many regions with features identical with those in the earlier specimens. Cellular pleomorphism, however, was evident in many areas and the previous arrangement in groups of cells was mostly replaced by diffuse growth. The pattern adopted was highly suggestive of malignant transformation, but neither the histological nor the clinical evidence was adequate to support a diagnosis of malignancy. No signs of visceral, lymph node, or bone metastasis were found at autopsy. Local recurrence after excision has previously been noted in only 11 of the some 300 carotid body tumors so far reported.

Clinical Aspects and Therapy of Temporal Arteritis. P. Lübbers and J. Edelhoff. Chirurg **26:**443-450 (Oct.) 1955 (In German) [Berlin, Germany].

This report is based on eight cases of temporal arteritis. The involvement of the temporal arteries is often only the most pronounced sign of a more generalized arteritis. The lesion is observed chiefly in elderly patients in the seventh and eighth decades of life. It is almost never observed in patients less than 55 years old. The main aspect of this disorder consists in inflammation of temporal arteries, which appear as swollen, indurated strands of the temples and may show no pulsation. The skin over almost pencil-sized arteries may be reddish. The severe temporal headache is characterized by some patients as throbbing, by others as piercing, and generally persists through day and night. Mechanical factors such as wearing of a hat or of glasses or the movements of the temporal muscles in chewing may increase the pain. In some of the patients swellings appear in the preauricular region that may suggest mumps; swelling around the eyes may suggest nephritis. These local symptoms may be accompanied by impairment in the general condition. The patients may be troubled by lack of appetite, nausea, loss of weight, excessive sweating, insomnia, and pains in the joints and extremities. The body temperature may be somewhat increased. The most important complication of the vascular process is the development of amaurosis as a result of damage to the optic nerve. This form of blindness may be unilateral or bilateral and is sometimes preceded by premonitory darkening before the eyes. The etiology and pathogenesis of the disorder have not been completely explained, but infections are held responsible by some, and for this reason chemotherapeutics and antibiotics have been used in the treatment. More recently corticotropin and cortisone are regarded as the most effective drugs. As regards relief of the temporal headaches, resection of a part of the temporal artery has been found most effective. This treatment was carried out in seven of the eight cases reviewed by the authors. Resection of a portion of the temporal artery counteracted the headache. Other advantages of the resection are that it corroborates the diagnosis and in many cases it may preserve the eyesight. The fact that resection of the temporal artery counteracts the pains is believed to be due to the fact that the arterial resection interrupts the pain-conducting centripetal fibers of the sympathetic. Although many surgeons recommend the removal of as much as 8 cm., these authors have generally limited the resection to a piece measuring from 2 to 3 cm.

The Pharyngeal Pouch. P. F. Howden. New Zealand M. J. **54:** 470-475 (Aug.) 1955 [Wellington, New Zealand].

The pharyngeal pouch occurs at the junction of the pharynx and esophagus. It is caused by some incoordination in swallowing that prevents relaxation of the cricopharyngeus muscle, and a pouch is formed posteriorly. The pouch is really a hernia between the oblique and horizontal sets of fibers of the inferior constrictor. Its wall consists of mucous membrane together with the fibrous coat of the pharynx and some muscle fibers spread as a thick collar around the neck. In commenting on the development of the lesion, the author mentions the opinions of other investigators, particularly those of Lahey and Warren, who recognized three stages in the development of the esophageal diverticulum. The author presents the histories of nine patients with pharyngeal pouches who were operated on at the Green Lane Hospital. Dysphagia, regurgitation, swelling in the neck, gurgle, cough, and loss of weight were the chief symptoms. The author feels that patients who have lesions corresponding to what Lahey regards as the second and third stages of the esophageal diverticula will require removal of the sac. His patients were subjected to the one-stage operation, which was condemned by Lahey and Warren, because of the danger of mediastinal infection following leakage, but the author feels that with antibiotics at hand this danger of infection is much diminished. A drainage tube down to the wound in the esophagus forms a track that will allow esophageal leakage to come to the surface if it should occur. The author describes his one-stage operative procedure for removal of the pouch. He uses a partial thyroid incision extending to the left over the sternomastoid but not extending fully to the right side. This allows adequate exposure of the left lobe of the thyroid. In cases where there is difficulty in locating the sac, a tube or packing can be passed into it from above. The sac is loosely adherent to the esophagus proper by fibrous tissue and has to be freed from below. The neck of the diverticulum is often firmly adherent to the esophagus, and care must be taken in freeing it so as not to perforate the esophagus. The most difficult part of the operation is to remove all the sac but not to remove any normal esophagus. A safe procedure is for the anesthetist to pass a wide bore tube down the esophagus and then the junction between the neck of the sac and esophagus proper can be found. The neck of the sac is severed at its uppermost point and a suture inserted approximating the edges of the mucosa of the esophageal opening. By a series of small snips with the scissors and the insertion of a suture each time, the esophageal opening is closed when the sac is removed, the sac being retained until the end as a retractor.

The Amount of Tissue to Be Preserved at Subtotal Thyroidectomy: An Estimate Based on Serial Isotope Tracer Measurements. D. E. Szilagyi, J. L. Barrett and L. E. Preuss. J. Clin. Endocrinol. **15:**1409-1421 (Nov.) 1955 [Springfield, Ill.].

The amount of thyroid tissue to be left in situ when thyroidectomy is performed for nonmalignant disease has hitherto been estimated largely by empirical guessing. Attempts have therefore been made to measure it quantitatively by studying the postoperative functional state of thyroid remnants in 25 patients subjected to subtotal thyroidectomy during a two-year period. The patients studied fall into three groups: (1) those with diffuse thyroid hyperplasia (Graves' disease), 10 cases; (2) those with toxic nodular goiter, 9 cases; and (3) those with nontoxic nodular goiter, 6 cases. Nontoxic nodular goiters were included mainly for purposes of comparison; in their surgical management the size of the remnant is not of great concern and usually depends on the type and extent of the pathological changes. More tissue was removed at operation than would ordinarily have been considered desirable, but, since it was necessary to use the trial and error method in attempting to determine the ideal size for the remnant, the amounts left in each group varied; in no case, however, were they large enough to be apt to cause persistent or recurrent hyperthyroidism. The size of the remnant was estimated by matching it as accurately as possible with a piece of tissue cut from a similar portion of the resected gland and then weighing the cut piece. Control measurements showed that this method of "matched weights" is accurate within a margin of

error of plus or minus 10%. Radioiodine tracer techniques and conventional clinical methods were used in studying the survival and rate of growth of the remnants and the relationship of changes in their functional state (i. e., avidity for iodine) to the clinical state of the patient. The patients were prepared for operation in the routine manner, except when preoperative I^{131} studies were made. Treatment after the operation also followed the usual pattern, except that no replacement therapy was given until at least two I^{131} tracer studies had been made. The tracer doses were given at intervals of from 3 to 6 months for periods ranging from 10 to 26 months, and the function of the remaining thyroid was investigated by clinical examination; by determination of the basal metabolic rate, the blood protein-bound iodine level, and the blood cholesterol level; and by I^{131} uptake and excretion studies. A definite and generally progressive increase in the capacity for iodine uptake was shown by 18 of the thyroid remnants; the other 7 were either exceedingly small or had a hypoplastic histological structure. The minimal amount of thyroid tissue required for the maintenance of euthyroidism was found to be much less than has hitherto been thought necessary, ranging from 0.8 gm. in diffuse hyperplastic goiter to 1.0 gm. in toxic nodular goiter. The deciding criterion used in classifying a patient's postoperative status was assessment of the clinical picture. Thus a patient with thyroid functional indexes in or even slightly below the lower normal range was designated as euthyroid if, without medication, he was symptom-free and showed no clinical signs of hypothyroidism. The results in these patients from the point of view of the success of the operations were very satisfactory. Longer periods of observation, however, will be needed before it can be stated whether thyroidectomies that leave only 800 to 1,000 mg. of parenchyma will lower the incidence of persistent or recurrent goiter. Radical procedures of this kind cannot be safely performed without a careful anatomic dissection of the gland, a gentle but sure definition of the recurrent laryngeal nerve, and the demonstration of at least one parathyroid body on each side.

Results of Conservative Operations for Malignant Tumors of the Thyroid. G. Crile Jr., J. G. Suhrer Jr. and J. B. Hazard. J. Clin. Endocrinol. **15**:1422-1431 (Nov.) 1955 [Springfield, Ill.].

Classification of the 182 malignant tumors of the thyroid seen on Dr. Crile's surgical service between 1937 and 1954 showed that 107 were papillary carcinomas, 8 encapsulated angioinvasive carcinomas, 7 medullary carcinomas, 15 adenocarcinomas, 28 undifferentiated carcinomas, and 11 miscellaneous in type. The patients with papillary carcinomas fell into two groups: 33 who had had a previous operation on the thyroid, referred to as the secondary group, and 74 who had had no previous operation on the thyroid itself, referred to as the primary group. Neck dissections or biopsies of cervical nodes had, however, been performed in 23 of the primary group patients. The definitive operation in more than half the patients in the primary group consisted of total lobectomy, with or without removal of lymph nodes. Total thyroidectomy was performed in only 12 (16%) of the cases, usually with bilateral removal of lymph-node metastases. Permanent tracheostomy was never necessary and permanent bilateral vocal cord paralysis did not occur. Recurrences, indicative of an incomplete initial operation, were present in 22 of the patients in the secondary group and in 19 of these both the thyroidal recurrences and the metastases in the cervical lymph nodes (18 unilateral) were removed. Operation was limited to lymph-node removal in the 11 patients without evidence of recurrence in the thyroid area. Two patients with distant metastases had cervical node biopsies only and one patient with diffuse local infiltration had a palliative excision of part of the thyroid tumor. Results in the secondary group were unsatisfactory when compared with those in the primary group. Four, possibly, five patients died of carcinoma and the incidence of distant metastases was 10 times as great in the secondary as in the primary group. The evidence, therefore, suggests that biopsy or partial excision often disseminates papillary carcinoma and renders it incurable. Complete excision of the primary tumor, on the other hand, with removal of grossly involved lymph nodes, produces excellent results: 61 patients so treated were living without any signs of recurrence at an average follow-up of 4.5 years. Determination of the end-results in 39 patients from both groups followed for five years or more after operation showed that 34 were living without evidence of carcinoma, one was living with distant metastases (present before operation), 3 had died of carcinoma, and one had died of other causes, with papillary carcinoma present at the time of death. The results of treatment of nonpapillary carcinoma of the thyroid depend much more on the type of the tumor than on the type of treatment. The percentage of successful end-results after five years or more in all types of tumors was 61.5; that is, 40 patients out of a total of 65 for whom determinate data were available were living without evidence of neoplasm. The findings in this survey seem to show that radical mutilating operations are rarely if ever indicated in the treatment of carcinomas of the thyroid.

Circumfereatial Suture of the Mitral Ring: A Method for the Surgical Correction of Mitral Insufficiency. J. C. Davila, R. P. Glover, R. G. Trout and others. J. Thoracic Surg. **30**:531-560 (Nov.) 1955 [St. Louis].

The reduction of the valvular ring by circumferential suture has several advantages over the principle of replacement of occluding valvular elements upon which practically all previously suggested techniques are based. These advantages include the fact that this procedure does not require the introduction of foreign materials across the lumen of the cardiac chambers. It makes full use of all remaining valvular substance capable of function. The effective orifice of the atrioventricular communication is not encroached upon by plugs or sutured cusps. It involves no more intracardiac manipulation than does a commissurotomy and results in no significant myocardial trauma. Not only does it make possible the elimination or reduction of regurgitation but it is plausible to expect that the size of the atrioventricular ring will be rendered incapable of progressive enlargement. This principle, with or without concomitant commissurotomy, appears applicable to most forms of mitral insufficiency. To investigate the problems associated with the correction of valvular insufficiencies by the circumferential constriction of the annulus, experiments have been made on some 150 dogs. A technique of correction has been evolved, and this report deals with a study of 80 animals in which this procedure has been used. The experimental work demonstrated that the regurgitation produced artificially can be eliminated. The procedure for circumferential suture or purse-string suturing of the mitral annulus in its present form has been proved to be relatively simple and safe. When properly performed, no significant damage to the cardiac conduction system, the coronary circulation, or the muscle itself can be demonstrated. No significant hemodynamic alterations can be attributed to the procedure in the experimental animals. Mitral stenosis is not produced. Clinical trial in seven severely ill patients demonstrated objectively and clinically that regurgitation associated with rheumatic heart disease can be corrected. The final results of this procedure would appear to depend upon the pathological state of the valve. The myocardial, pulmonary, hepatic, and renal status of the severely ill patients who have been operated upon appears to be the major cause of death in the three patients who died. Continued clinical trial seems justified. Until further experience has been acquired, however, the procedure should be applied only in critically ill patients. Although the technique in its present form is simple and easy to perform, a preliminary study of the pertinent anatomy and practice on experimental animals will be essential for its proper performance.

Combined Radiotherapy and Resection for Carcinoma of the Bronchus: Experiences with 66 Patients. L. L. Bromley and L. Szur. Lancet **2**:937-941 (Nov. 5) 1955 [London, England].

Pulmonary resection offers the best hope of permanent cure in carcinoma of the bronchus, but it is applicable to only a small proportion of patients. The results of surgical and radiological treatment are not strictly comparable since favorable cases are generally subjected to surgery and radiotherapy is tried in unfavorable cases. The authors combined radiotherapy with surgery. They organized a bronchus tumor clinic attended by radiotherapists, chest physicians, and thoracic surgeons. Each patient

was assessed on clinical, radiological, and bronchoscopic grounds and placed in one of several groups according to operability, various causes of inoperability, and recurrence. Five hundred and seventy-three of the 732 patients who attended the clinic were treated. Radiotherapy was given with voltages between 190 and 250 kv. Tumor and skin doses were estimated individually. Treatment was based on multiple small fields using careful beam direction. A coplanar field arrangement was employed. The number of fields varied from 5 to 10; field sizes were 6 × 8, 5 × 10, or 8 × 10 cm. The dose aimed at was 5,000 to 5,500 r in five to six weeks. In practice the tumor dose varied between 3,700 and 6,000 r, the average in the 66 patients being 4,700 r. The time taken to complete the course of treatment varied between 32 and 50 days. When radiotherapy was completed, a further bronchoscopy was performed. After a period of convalescence, a further assessment was made and, if the condition was considered operable, the patient was advised to submit to thoracotomy. This paper is concerned with those 66 patients (58 men and 8 women) who underwent resection. The average time between the first attendance at the clinic and the start of radiotherapy was 19 days and between the completion of irradiation and operation 74 days. The pleural cavity was entered usually through the bed of the resected sixth rib. No particular technical difficulties were encountered, although in some cases it was the surgeon's impression that the hilar structures were surrounded by more adherent fibrous tissue than usual. This made dissection of the vessels sometimes difficult but not unusually formidable. The operation was a pneumonectomy in 64 patients and a lobectomy in 2. The tumor had apparently been eradicated from the chest in nearly half the cases, but there was a high incidence of empyema and fistula. The results produced by the combination of radiological and surgical therapy were not impressive. Ten patients died at operation, 38 died with cancer, 5 of intercurrent disease, 2 are alive but have cancer, and 11 are alive and free from cancer.

Immediate and Long-Term Results of Pulmonary Exeresis for Tuberculosis. J.-F. Nuboer. Bruxelles-méd. **35:**2223-2234 (Nov. 6) 1955 (In French) [Brussels, Belgium].

The author stresses that pulmonary exeresis for tuberculosis should be performed only after medical treatment of the disease has been unsuccessful. A great deal of the success of the operation depends on its being carried out at the proper moment, that is, at a time of inactivity of the tuberculous process. The resection cannot be expected to rid the body of all diseased tissue, but only of enough of it to enable the body's natural forces to operate toward healing. The present series of 1,036 resections comes from Utrecht, Netherlands, where this operation is used only in about 30% of sanatorium patients. One thousand twenty-four of the operations were carried out under antibiotic and chemotherapeutic coverage; 16 patients of this group died, and 3 of the remaining patients, making the operative mortality rate for the 1,036 exereses 1.8%. Bilateral resection was performed in 29 instances, without mortality. The mortality rates for the various kinds of operation were: pneumonectomy, 4.6%; lobectomy, 2.2%; and segmental resection, 0.22%. The late mortality among the 1,017 patients having survived operation was 17, a rate of 1.6%. Among the 1,008 patients surviving in the operation-with-coverage group, 84 later had complications directly connected with their tuberculous disease. Nine of them died, 25 remained unwell, 13 were cured by conservative treatment, and 37 were cured by reintervention. Loss of pulmonary function was minimal in this series, and this feature is in fact one of the three great advantages of pulmonary resection over collapse therapy and thoracoplasty, the other two being the great chance of cure and the small mortality.

Significance of Parasternal Lymph Nodes (So-Called Mammary Lymph Nodes) with Regard to Spread and Prognosis of Mammary Carcinoma. E. Kaiser. Schweiz. med. Wchnschr. **85:** 1073-1075 (Oct. 29) 1955 (In German) [Basel, Switzerland].

Of 40 women with cancer of the breast who were subjected to radical mastectomy at the surgical department of the Waid City Hospital in Zürich, Switzerland, in whom the parasternal lymph nodes along the internal mammary artery were removed at the same time, these lymph nodes proved to be carcinomatous in 9. Of the 40 tumors, 11 were medial and 29 were lateral. Two of the 11 tumors had metastasized in the mammary lymph nodes, and 7 of the 29 did. The rate of involvement of the mammary lymph nodes thus was 23%; a review of the literature showed that depending on the location of the tumor the parasternal lymph nodes may be involved in 20 to 40% of the cases. The relatively high percentage of involvement of the parasternal lymph nodes makes it imperative to remove these nodes simultaneously with the mammary gland, the sternocostal two-thirds of the major pectoralis muscle, and the entire axillary fat depot with its lymph nodes and to remove the parasternal lymph nodes and the other organs independently of any other procedure, i. e., whether or not the radical mastectomy is preceded or followed by roentgen irradiation. It is not certain whether the roentgen rays will completely destroy the axillary lymph nodes, and this is much more doubtful regarding the parasternal lymph nodes that are much deeper embedded (up to 2.5 cm.) and are situated partly under the costal cartilage. The technique of the removal of the parasternal lymph nodes is simple, provided that intratracheal anesthesia is available, which removes the risk from opening up the pleura that occurred in four patients. There are good reasons for combining the mastectomy with removal of the axillary lymph nodes, but the same reasons hold good for the removal of the parasternal lymph nodes, since both groups of lymph nodes are the first to be involved by the tumor. Statistics collected from the literature show a 60% five-year cure rate of patients with carcinoma of the breast who underwent radical mastectomy with removal of parasternal lymph nodes, as compared to a 47% five-year cure rate of patients who underwent radical mastectomy and postoperative irradiation. Extirpation of the so-called mammary lymph nodes should be an essential part of the operation in every case of carcinoma of the breast.

Present Status of Thymectomy in Treatment of Myasthenia Gravis. L. M. Eaton and O. T. Clagett. Am. J. Med. **19:**703-717 (Nov.) 1955 [New York].

The authors review critically the more significant reports of recent years on the value of thymectomy against the background of earlier contributions and compare them with observations on Mayo Clinic patients with unquestionable myasthenia gravis and on some in whom thymectomy was performed. They arrive at the conclusion that thymectomy is of value in the treatment of female myasthenic patients who are less than 50 years of age and who do not have thymomas. Too few patients who are alike, except that they are more than 50 years of age, have been studied to allow the formation of definitive conclusions. Younger female patients surviving thymectomy have better than a 50% chance of attaining very satisfactory remissions, whereas without thymectomy they have a 20 to 25% chance of attaining comparable results. The chances of ultimate survival of patients in this group are substantially increased by removal of the thymus gland. The authors approve of thymectomy in the case of female patients, particularly if they are young, in spite of the fact that surgery in severe degrees of myasthenia gravis is of great risk to the patient. It is probably not wise to advise thymectomy, even in female patients, if the disease has been present for many years (10 or more), particularly if it is stationary or improving. The value of thymectomy in male patients has not been demonstrated conclusively, but the authors approve, tentatively, of offering thymectomy to male patients as of potential benefit unless the risk of surgery contraindicates the use of a procedure the worth of which is not yet conclusively established for such patients. Thymectomy for removal of thymic tumors carries a relatively great risk to the patient and is not of proved value, although data in studies of the Mayo Clinic series suggest that it may be effective in female patients. Perhaps it should be undertaken provided there is no clinical or roentgenologic evidence of inoperability and the risk of surgical intervention does not appear excessive. Otherwise a patient who is destined to do well as far as myasthenia gravis is concerned may die as a result of thymoma. Roentgen therapy is reserved for those patients who are unsuited for surgical treatment.

Multiple Polyposis of the Colon, Osteomatosis and Soft-Tissue Tumors: Report of a Familial Syndrome. R. S. Weiner and P. Cooper. New England J. Med. **253:**795-799 (Nov. 10) 1955 [Boston].

The authors treated three brothers with an unusual combination of abnormalities. The brothers had multiple polyposis of the colon, osteomatosis, and multiple soft-tissue tumors. All three patients were subjected to ileostomy and total colectomy. The resected intestine specimens revealed adenocarcinoma of the rectum or colon, or both, in two, in addition to the multiple polyposis. A fourth brother, who was hospitalized and studied elsewhere, had an ileostomy and total colectomy performed for multiple adenocarcinomas of the large intestine. X-ray examination of the skull showed multiple exostoses. No soft-tissue tumors were found. The relatives of the brothers could not be studied because of lack of cooperation. In reviewing the literature the authors found that Gardner and his associates in 1951 had reported multiple cutaneous and subcutaneous lesions occurring simultaneously with multiple polyposis of the colon and osteomas in 6 members of a family group of 51 living persons, and one member, a child, had only subcutaneous tumors. There were three types of cutaneous or subcutaneous tumors: epidermoid cysts, fibromas, and poorly defined masses of connective tissue. The lesions occurred on the head, back, chest, and abdomen and extremities. They were always multiple. Eight family members, then deceased, were reported to have died of cancer of the colon and rectum; six of these persons were reported to have had osteomas, and all eight were known to have had subcutaneous tumors or cysts. Gardner and his associates concluded that a single defective gene with a dominant mode of inheritance was the most likely explanation for the presence of all three abnormalities in the family group studied. The authors believe that the brothers observed by them are the second family in which this syndrome has been reported. Carcinoma of the colon is just as likely to develop in patients with this syndrome as in those with the more common variety of multiple polyposis of the colon. X-ray examination of the bones of all members of any family in which this syndrome appears may help determine in which members polyposis will develop, for the bony changes may be the first manifestation of this disease. It should also be realized that fibrous-tissue tumors may develop in any incisions in these patients.

Repair of the Surgically Injured Ureter. T. H. McDonell. Wisconsin M. J. **54:**497-500 (Oct.) 1955 [Madison, Wis.].

Surgical injuries of the ureter are surprisingly common and have been produced by the most skillful surgeons. Ureteral trauma usually occurs in the course of complicated gynecologic procedures. The injury, therefore, is low in the ureter. This has the obvious disadvantage of limiting exposure during attempts at repair. However, the low level of injury does leave a long proximal segment of ureter, which facilitates transplantation when necessary. About one-sixth of surgically induced ureteral injuries involve both ureters. Surgical trauma to the ureter may take many forms. The ureter may have been enveloped by a single ligature. A suture ligature may have perforated the lumen. The ligature may have been so placed in close apposition to the ureter that resulting angulation proves obstructive. The ureter may have been cleanly severed, or only a part of its wall may have been excised. The ureteral blood supply may have been so compromised that necrosis occurs. On occasion, a considerable length of the ureter may have been crushed or excised. If the surgeon is fortunate enough to recognize the ureteral injury at the time of surgery, repair can be carried out immediately. Ureteral continuity can usually be reestablished. Several days may elapse before the injury causes symptoms. Bilateral complete obstruction will, of course, produce total anuria and, soon thereafter, uremia. Unilateral incomplete obstruction will usually result in a slowly developing hydronephrosis. An uncomplicated hydronephrosis usually produces an ill-defined flank discomfort and only occasionally outright pain. The symptom complex may be entirely gastrointestinal in character. Infection is of grave consequence. Fever and chills are prominent. Flank pain and tenderness are exaggerated. An acute hydronephrosis that becomes infected usually means rapid renal destruction. When ureteral continuity is interrupted, a fistula has been produced and extravasation results. The only worthwhile preventive measure is the passage of ureteral catheters preoperatively whenever difficult pelvic surgery is anticipated.

Treatment of Pseudarthrosis by Phemister's Subperiosteal Onlay of Bone Grafts or by Intracortical Placement of Bone Grafts. U. Ritter. Zentralbl. Chir. **80:**1105-1115 (No. 28) 1955 (In German) [Leipzig, Germany].

To stimulate and utilize the "osteogenetic potentialities" within the bone for the treatment of pseudarthrosis, Ritter uses the method of intracortical placement of a bone splinter. He cuts down to the bone without separating the connections of skin, subcutaneous tissue, fascia, musculature, and periosteum. With the bone knife he cuts into the periosteal tube, but instead of lifting the periosteum he prepares the intracortical bed for the bone splinter graft by chiseling off the outer lamellae of the bone cortex, with the aid of a Lexer chisel in the direction of the pseudarthrosis, in such a way that they adhere to the periosteum. The newly formed bony projections and marginal proliferations in the region of the pseudarthrosis are not removed. The increase in volume resulting from the introduction of the splinter makes the closure of the periosteum impossible; anyway, this is no longer regarded as necessary. Tight closure of the fascias, however, is always possible, and prevents tension in the skin. The author illustrates the value of this method on the basis of several case histories. He compares this method with others that have been recommended for the treatment of pseudarthrosis such as Beck's simple drilling, Kirschner's splintering, and particularly Phemister's subperiosteal onlay of bone grafts. While his method has much in common with Phemister's subperiosteal bone onlay grafts, he feels that it combines the advantages of Phemister's method with Kirschner's method of splintering.

Monteggia Fractures. J. E. Mobley and J. M. Janes. Proc. Staff Meet. Mayo Clin. **30:**497-504 (Nov. 2) 1955 [Rochester, Minn.].

The injury characterized by fracture of the shaft of the ulna and associated with dislocation of the head of the radius is known as a Monteggia fracture. It is a relatively rare injury that has proved very difficult to manage because of the frequency of complications. Depending upon the direction of dislocation of the head of the radius, Monteggia fractures are classified as anterior, posterior, and lateral. Of the 15 patients with Monteggia fractures who were seen at the Mayo Clinic between 1930 and 1954, 10 had anterior, 2 posterior, and one a lateral type of fracture. In the other two the type could not be determined. Ten of the 15 patients had new fractures, and in 5, from 1 to 13 years had elapsed since the fracture. Complications were common; in order of frequency they were: nonunion of the ulna, traumatic arthritis, persistent dislocation of the radial head, peripheral nerve palsy (temporary), and cross union of the radius and ulna. The final results of treatment could be evaluated in 10 of the patients; they were excellent in one, good in 6, fair in 2 and poor in one. Monteggia fractures in children usually can be treated by manipulation and immobilization without operative intervention. Occasionally, open reduction will be necessary for replacement of the head of the radius, which never should be excised in children. The final results in children generally are better than in adults. An anterior or lateral Monteggia fracture in an adult person probably is best treated by open reduction of the ulnar fracture and manipulative reduction of the head of the radius. Should manipulative reduction of the head of the radius fail, the radial head can be replaced surgically either at that time or later. After reduction has been accomplished, the extremity should be immobilized for 8 to 12 weeks or longer, with the elbow at a right angle and the forearm in midposition. Immobilization must not be discontinued too soon, because premature freeing of the parts increases the risk of nonunion. The posterior Monteggia fracture is best managed by manipulation and immobili-

zation, with the elbow in complete extension. Nonunion of the ulna can be managed by bone-grafting procedures. Excision of the radial head may be necessary for persistent dislocation or traumatic arthritis.

NEUROLOGY & PSYCHIATRY

Chlorpromazine, Reserpine, and Isoniazid Treatment in Mental Disorder: A Preliminary Communication. J. K. Hewat, P. W. W. Leach and R. W. Simpson. Brit. M. J. **2**:1119-1120 (Nov. 5) 1955 [London, England].

Sixteen patients, eight men and eight women, with chronic psychoses and of widely varying somatic and physiological types, were given orally a compound preparation containing 25 mg. of 10-(3-dimethylaminopropyl)-2-chlorphenothiazine (chlorpromazine), 1 mg. of reserpine, and 50 mg. of isoniazid. Beginning with one tablet, the dose of the drug was increased every day until four tablets daily were given. The treatment lasted three weeks. Side-effects were as follows: A definite fall in blood pressure by more than 20 mm. systolic or 10 mm. diastolic occurred in 8 patients; nasal congestion in 3, dryness of mouth in 2, pallor in 6, flushing in 4; parkinsonism in 6, tremor in 4, drowsiness in 11, insomnia in one, giddiness in 2 and headache in one. An increase in weight occurred in 12, and a loss of weight in 2. Pains in trunk and limbs occurred in four, malaise and weakness in eight, and shivering in nine. All these side-effects subsided within a few days of discontinuation of the drug. No abnormal hematological or unequivocal biochemical changes were observed. In view of the unexpectedly high incidence of extrapyramidal signs, another therapeutic trial with the same compound preparation, but in a smaller dose, was carried out on another group of 16 patients who were given 50 mg. of chlorpromazine, 2 mg. of reserpine, and 100 mg. of isoniazid daily for four weeks. Hypotensive and bradycardic trends similar to those in the first trial were noted. Nasal congestion occurred in two, dryness of mouth in two, and flushing in one. Parkinsonism was observed in none of the patients, tremor in one, drowsiness in three, giddiness in two, and headache in none. An increase in weight occurred in 11 and weight loss in one. Malaise and weakness occurred in two, pains in trunk or limbs in one, and shivering in three. As in the first trial, all side-effects subsided rapidly when treatment was stopped. No abnormal hematological or biochemical changes were observed. Although the duration of treatment was too short and the number of patients too small for a final evaluation, the authors' preliminary observations suggest that the combination of the three drugs used had a definite effect on the patients' mental state. In the first trial, four patients became much worse, three worse, five did not show any change, and four were improved. In the second trial with the combination of drugs in smaller doses, one became much worse, two worse, three showed no change, seven were improved, two were considerably improved and in one treatment is still in progress. In the patients who were benefited by the treatment, the trend was towards a quieter, more cooperative, and more relaxed state. Although parkinsonism is known to occur with chlorpromazine and reserpine when used singly in large doses, its occurrence with small doses in combination was unexpected, and it is suggested that they might have a potentiating action. This action may have therapeutic significance. Apart from a slight modification in dosage, the authors' preliminary trials with combination of chlorpromazine, reserpine, and isoniazid did not reveal any contraindication to proceeding with the investigations of the individual and combined therapeutic effects of these drugs in psychiatry.

A Comparison of Chlorpromazine and Reserpine in Chronic Psychosis. B. Kovitz, J. T. Carter and W. P. Addison. A. M. A. Arch. Neurol. & Psychiat. **74**:467-471 (Nov.) 1955 [Chicago].

The authors investigated the following problems: (1) the effect of chlorpromazine and reserpine in chronic psychosis, particularly in schizophrenia; (2) syndromes in which these drugs are most useful; (3) their relation to other methods of treatment, and (4) their comparative advantages and disadvantages. The studies were made on 150 patients with an average period of hospitalization of 6.6 years. The illness of these patients had not responded well to the usual therapeutic methods. Half of the patients required maintenance electric convulsive therapy during the seven months preceding this study. The group included 127 cases of chronic schizophrenia. The remainder consisted of cases of chronic or relapsing manic psychosis, depressive psychoses, and chronic brain syndrome with affective or convulsive disorder. The 150 patients were divided into three matched groups of 50 (25 of each sex). Group A received placebos throughout the 16-week experiment. Group B received reserpine for six weeks and chlorpromazine for six weeks. Group C received chlorpromazine for six weeks, placebos for four weeks, and reserpine for six weeks. Reserpine was used in doses of 2 to 5 mg. daily. Chlorpromazine was used in doses of 100 to 400 mg. daily, except in a small number of cases in which up to 650 mg. was given daily. Electric convulsive therapy was suspended, with the understanding that the ward physician could apply it whenever he considered the patient disturbed enough to make it necessary. Improvement was found in 53% of cases of severe chronic schizophrenia treated with reserpine, in 58% of such cases treated with chlorpromazine, and in 24% of similar cases treated with placebos. Patients treated with placebos also required about three times as much electroconvulsive therapy. Electroconvulsive therapy may be effectively combined with reserpine or chlorpromazine, and fewer treatments are required to achieve symptomatic benefit. Chlorpromazine and reserpine both tended to decrease muscle tension artifact in the electroencephalogram. Chlorpromazine produced a sustained increase in serum bilirubin in many patients without overt jaundice. Reserpine acts more slowly. Its side-effects are apt to be unpleasant but seldom serious. It tends to diminish the quantitative intensity of pathological affects, rather than to change them qualitatively. Chlorpromazine acts more rapidly. Side-effects are less unpleasant but may require stopping the medication. It is relatively ineffective in depression. It tends to induce qualitative and quantitative improvement in states of anxiety, tension, and hostility. Chlorpromazine and reserpine produce essentially symptomatic improvement through less intense or impulsive expression of emotion; they influence the motor-affective more readily than the ideational sphere. Results with these drugs are best in patients with persistent evidence of tension, strong affect, and efforts to maintain self-esteem. Both drugs are of particular value for the patient with chronic, relapsing, but nondeteriorating schizophrenia who could not otherwise adjust successfully outside the hospital.

Factors Favoring the Curative Effect in Psychoanalytic Therapy. H. Meng. Schweiz. med. Wchnschr. **85**:1096-1099 (Nov. 5) 1955 (In German) [Basel, Switzerland].

The observations presented are the fruit of long experience, since the author has been a physician since 1912 and a phychoanalyst since 1920. Psychoanalysis is not a panacea, nor can it work miracles. In some disturbances, however, it is the only possible and in others the most effective treatment, but it cannot accomplish anything without expenditure of time and effort. In some cases the method produces no therapeutic effects but provides a certain amount of understanding, which may prepare the way for a later more direct influence on the neurotic disturbances. Psychoanalytic procedures are indicated chiefly in all transference neuroses, such as hysteria and compulsion neuroses, in which they uncover the internal structures and mechanisms, but also in all types of phobias, inhibitions, character deviations, sexual perversions, and difficulties in the love life. Since psychoanalysis requires a measure of psychic plasticity in patients, its use should be restricted to a certain age limit. The author is not able to give a definite answer to the question as to what produces the therapeutic effect in psychoanalysis but suggests that the capacity for normal experience is restored. The super-ego is rendered more stable, more tolerant, more realistic, more experienced, and more open and free than it was before. Particularly the capacity to love is changed in this process of transformation. The healthy ego learns to put realism ahead of the pleasure principle. The patient becomes capable to free himself from the Oedipus constellations of early childhood. Neurotic anxieties

are overcome. Factors that seem to be particularly important for the curative effect of psychoanalysis include among others: (1) the normalized interpersonal constellations of the analytical situation in the subconscious and the conscious; (2) the shock effect of the "now-I-see" experience in the process of self-understanding; (3) the new capacity for experiences in environmental relations, particularly in making contacts, experiencing distance, and in acquiring tact; (4) tolerance for rejection and acceptance; (5) the exemplary bearing of the analyst; (6) the new attitude toward life and death, transitoriness, and relativity; (7) freedom for the supremacy of the intellect; (8) the capacity and the fortitude to accept what one knows; (9) the realization that life for the ego is synonymous with being loved by the super-ego, and (10) formation of a new super-ego during the interpersonal relations in the process of transference. The author also discusses Freud's attitude to philosophy and religion. He shows that Freud was an empiricist and opposed to all ideologies. His studies on the etiology of the feeling of guilt are of interest for the psychology of religion and for the treatment of nonreligious neurotics.

GYNECOLOGY & OBSTETRICS

Rupture of the Pregnant Uterus. T. F. Bak and G. E. Hayden. Am. J. Obst. & Gynec. **70**:961-971 (Nov.) 1955 [St. Louis].

Fifty-two cases of rupture of the uterus occurred among 71,483 deliveries from 1931 to 1953. The associated maternal mortality was 15% and the uncorrected fetal mortality was 50%. Uterine rupture remains a serious surgical emergency, but there were no maternal deaths in the 21 ruptures that occurred from 1942 to 1953. The following factors were responsible for this reduction in maternal mortality: better understanding of the physiology of labor, hospital delivery, earlier diagnosis, more adequate blood and fluid replacement, immediate surgical intervention, and employment of antibiotics. Forty-five per cent of the traumatic uterine ruptures resulted from version and extraction. Stricter adherence to the indications and conditions required for the obstetric procedure and the more liberal use of cesarean section were the most important factors in the prevention of rupture. Fifteen cases of uterine rupture occurred in patients with previous cesarean sections, this being 1.0% of the patients with a previous section who came to term. The policy of once a section always a section is strongly advised. Prevention by the properly selected obstetric operation is better than treatment. When a rupture of the uterus is suspected, the management of choice is early diagnosis by manual exploration of the uterine cavity and visual inspection of the vagina, cervix, and lower uterine segment, judicious blood and fluid replacement, and surgical treatment. In most instances a subtotal hysterectomy offers the most rapid control of hemorrhage with minimal trauma.

The Effect of the Stage of Gestation and Number of Pregnancies on Susceptibility to Poliomyelitis. L. Weinstein and R. H. Meade III. Am. J. Obst. & Gynec. **70**:1026-1032 (Nov.) 1955 [St. Louis].

The wide exposure to the poliomyelitis virus results in subclinical immunization of large numbers of persons. The more frequent occurrence of clinical poliomyelitis under particular circumstances and in certain individuals is suggestive of mechanisms of susceptibility related to the host rather than to the nature of the virus. Although previous exposure with the development of immunity plays a major role, there appear to be various nonspecific host factors that are determinants not only of susceptibility to viral invasion but probably also of the course and outcome of the disease once infection has occurred. The authors investigated the various possible factors in 60 pregnant women whom they observed in the acute phase of poliomyelitis. It was found that at the onset of poliomyelitis 14 patients were in the first, 30 in the second, and 16 in the third trimester of pregnancy. The development of the paralytic type of pregnancy was largely independent of the period of pregnancy, except that vulnerability to paralysis was greatest in the fifth and seventh months of gestation. The relationship between the age of the patients and the trimester of pregnancy in which they appeared to be most susceptible to poliomyelitis was analyzed. There was very little difference in the prevalence of poliomyelitis in the first two trimesters in the youngest age group (20 to 24 years) while in those aged 25 to 29 the disease occurred most often in the last three months. In women 30 to 36 years of age, poliomyelitis was most frequent in the last trimester. These findings suggest that age may be an important factor in determining susceptibility to poliomyelitis in various trimesters of pregnancy and that studies of the effect of the duration of gestation on the incidence of this disease may yield different results unless the age distribution of the patients is taken into consideration. Multigravidity seems to increase susceptibility to poliomyelitis; paralysis was present most often in women pregnant for the second time. Older age seems to accentuate the increased susceptibility to poliomyelitis associated with multigravidity.

Visceral Hemorrhages in Hyperfolliculinism. H.-P. Klotz, Caen and Durlach. Semaine hôp. Paris **31**:3444-3449 (Nov. 6) 1955 (In French) [Paris, France].

Eleven cases of hemorrhages associated with hyperfolliculinism are described. A causal relationship between the two disorders seemed logical because relapses occurred in the premenstrual period, there were clinical and laboratory signs of hyperfolliculinism in each instance, no organic cause could be found after a thorough search, and the hemorrhagic syndrome was benefited by antifollicular hormone treatment. Four of the patients had digestive hemorrhages, five hematuria, one hematuria and hemoptysis, and one various visceral hemorrhages (hematuria, rectorrhagia, menometrorrhagia, gingivorrhagia, and epistaxis). Most of the patients showed a lowering of capillary resistance and a certain tendency to hypocoagulability. The condition is rather rare, but awareness of it may save a future patient a needless operation like the nephrectomy performed in one patient of this series. Effective therapy consists of a combination of testosterone, progesterone, and α-tocopherol. It is reemphasized that the diagnosis of hemorrhages due to hyperfolliculinism cannot be made until all possibilities of local causation have been most carefully excluded.

Cervical Pathology and Sterility Problems. C. L. Buxton. Connecticut M. J. **19**:864-870 (Nov.) 1955 [New Haven, Conn.].

Buxton calls attention to the paucity of information regarding the role of the cervix in sterility. Early investigators were impressed by the possibility that a tight external or internal os and small cervical canal might be an infertility factor, and cervical dilatations were carried out for the purpose of increasing the size and diameter of the cervical canal. Now, however, it seems doubtful if the tightness of the internal or external os or the narrow diameter of the cervical canal have anything to do with infertility, except in rare instances. The author also doubts that certain abnormalities in the position of the cervix are of significance in infertility, unless they are extreme. The cervix is a factor in sterility chiefly because of pathological changes in the physiology, the chemistry, and possibly the bacteriology of the cervical canal. One of the most interesting physiological changes is the cyclic change in the cervical mucus. During the first part of the cycle, after the cessation of the menstrual flow, the cervical mucus is scanty, thick, and viscous, with a low acid pH and a high cellular content. A day or two before ovulation, or in a normal 28 day cycle at about the 12th day, the heavy white cell infiltration of the previous days disappears, the mucus becomes much more hygroscopic, and thus its flow elasticity becomes much greater and its viscosity much thinner. The pH of the cervical mucus changes to an alkaline level, and the chemistry of the mucus also changes so as to acquire a considerable content of mucoprotein and polysaccharide. All these changes result in a medium that is admirably suited to sperm migration. With regard to the role of the bacteria present in the cervix, it is pointed out that organisms found in the cervical canal, although spermicidal in vitro, are not necessarily spermicidal in vivo. In the presence of chronic cervical catarrh, however, infection must be cleared up to produce normal mucus and remove a barrier to conception.

PEDIATRICS

Fatal Tuberculosis from BCG Vaccination. S. Falkmer, A. Lind and L. Ploman. Acta pædiat. **44:**219-236 (May) 1955 (In English) [Uppsala, Sweden].

An 8-month-old baby boy was vaccinated with BCG vaccine, intradermally, in the left thigh, a few days after birth. Regional lymphadenitis developed in the infant at the age of 6 months and was followed by a progressive, emaciating disease that proved resistant to therapy. Chest roentgenograms revealed large infiltrations in the left superior lobe and at the bases of both lungs, and minor infiltrations above the right hilum. The patient's reaction to the tuberculin test was negative. The patient died and autopsy showed widespread tuberculosis of atypical appearance with extensive involvement of lymph nodes. Myriads of acid-fast bacilli were found at the site of vaccination and in the regional, mesenteric, and retroperitoneal lymph nodes. Smaller numbers of acid-fast rods were found in the thymus, spleen, liver, and in the upper lung lobes, in which a peculiar type of pneumonia was observed. The spread of the disease was principally lymphogenous. The bacteriological investigation of cultures taken at autopsy showed that the disease was caused by a low-virulent strain of acid-fast bacilli, indistinguishable from BCG. Additional cases of fatal tuberculosis in a 15-month-old girl, a 9-year-old boy, and a 24-year-old man, all three from Scandinavian countries, who had been vaccinated with BCG a few days after birth and at the ages of 7 and 4½ years, respectively, were collected from the literature. The clinical course did not show any specific signs differing from those of common severe tuberculous infection. The reaction to the tuberculin test was faintly positive in one and negative in two. Pathologically, the four cases had many features in common and in the three children the findings differed in several respects from those encountered in fatal tuberculosis in children caused by Mycobacterium tuberculosis. The clinical aspect was predominantly one of widespread tuberculosis of lymph nodes, mostly of a noncaseous type, with myriads of acid-fast bacilli in the parenchyma. Despite the great enlargement of the lymph nodes, they showed no nodular tissue reaction, no formation of giant cells, and practically no caseous necrosis. These are features seldom observed either in the lymph nodes of the primary complex or in common lymph node tuberculosis. The unusual findings in the lymph nodes are those to be expected in young persons with faint tuberculin hypersensitivity, or with none at all, and with poor resistance, infected with a strain of tubercle bacilli of low virulence. The lungs showed widespread lesions of atypical appearance both macroscopically and microscopically. Most alveoli contained fibrinous material. Large numbers of monocytes without epitheloid appearance and alveolar macrophages, smaller numbers of lymphocytes, plasma cells, and eosinophilic and neutrophilic granulocytes were found. In many places the alveolar exudate was beginning to organize. The small bronchi were somewhat ectatic with denuded epithelium. There was a fairly marked edema around the larger vessels. The alveolar septums were thickened and fibrotic and were infiltrated with the same inflammatory cells as the contents of the alveoli. From the pathological as well as from the clinical point of view it is highly probable that the patients who obviously died of "BCG-itis" were in a poor state of resistance against infection. A low resistance constitutes a lack of physical equipment, which, however, might not often be obvious at the time of vaccination and is thus of limited value as a possible clinical contraindication to vaccination. The four fatal cases do not overbalance the many million vaccinated without complication. The prophylactic value of the vaccination is too great for it to be omitted in a tuberculous environment. When the tuberculous threat is less obvious, the complications must play a major role. Even if they are rare, their number is not negligible when the whole population is vaccinated.

Should Mass Vaccination with BCG Be Discontinued in Scandinavia? A. Wallgren. Acta pædiat. **44:**237-253 (May) 1955 (In English) [Uppsala, Sweden].

Natural nonspecific resistance against tuberculosis is the most powerful factor in protection against tuberculous disease and is probably the only determinant for the development of the most frequent, and, from a mortality point of view, the most important form: postprimary pulmonary tuberculosis. Specific immunity seems to have little or no influence on the degree of resistance against this disease. The specific immunity produced by a tuberculous infection is stronger than the immunity after artificial BCG infection. Therefore, there is no reason to believe that BCG vaccination could decrease the morbidity rate of postprimary pulmonary tuberculosis any more than the specific immunity after primary tuberculous infection. The decline of tuberculous morbidity and mortality from pulmonary tuberculosis in a country, therefore, cannot be caused by BCG mass vaccination. Specific immunity is more or less effective against the immediate consequences of new exogenous infections. Comparison of vaccinated and unvaccinated groups shows that the vaccinated are to a high degree protected against clinical primary tuberculosis and to a certain degree also against the early postprimary diseases, namely, miliary tuberculosis, meningitis, pleurisy, and local progression of primary tuberculous lesions of the lungs. The increased resistance produced by BCG immunity is of the greatest value in age groups with a very low natural resistance, i. e., infants and small children, and in children who run the evident risk of being exposed to tuberculous infection. In a country with a very high tuberculous morbidity, all children are in danger of being exposed and most of them are infected, many at a very early age. In such a country, the need of BCG mass vaccination should be emphasized and vaccination performed on all tuberculin negative children—the sooner the better in order to protect infants and small children. In a country with a very low tuberculous morbidity, only a few children are infected by sources of infection in the home surroundings, most of them not before school age, i. e., at an age with high natural resistance. In such a country, the need of mass vaccination may be justly questioned because only a minute fraction of all vaccinated become exposed. Most of the children have never had an opportunity to profit by BCG immunity and have thus been unnecessarily vaccinated, with all the cost and inconveniences this procedure may imply. BCG vaccination should be confined to selected groups in the population who are in danger of being infected (home contacts, nursing personnel, medical students, conscripts). The severe or fatal accidents and complications after BCG vaccination that have recently been reported from the Scandinavian countries make it still more desirable to reconsider the present principles of BCG vaccination in countries with a very low morbidity and mortality of tuberculosis.

Streptococci and Infectious Nephritis. R. Wahl. Presse méd. **63:**1366-1368 (Oct. 15) 1955 (In French) [Paris, France].

Acute nephritides, including the one associated with scarlet fever, are usually a consequence of infection of the upper respiratory tract with a group A beta-hemolytic streptococcus. The incidence of these nephritides varies widely according to locality, season, and year but is not correlated with the incidence of streptococcic infection in general or that of other complications, such as acute articular rheumatism. Sometimes veritable epidemics of nephritis occur. These unexpected variations are explained by the fact that, of the 40 types of streptococci in group A, there is one, type 12, that is peculiarly nephritogenic. Certain other types probably also play a role. The usual lack of relapses in connection with the disease is explained by the particular form of immunity, i. e., an immunity to the type, conferred by infections with group A streptococci. Type 12 infections should be treated intensively and as early as possible, so that nephritis may be prevented. Experimentally, it has been possible to reproduce a nephritis by infecting rabbits with type 12 streptococci.

The Value of Splenectomy in Fanconi's Anemia. R. C. Francis, R. A. Moir and P. N. Swift. Arch. Dis. Childhood **30:**439-444 (Oct.) 1955 [London, England].

Fanconi's anemia was observed in an 8-year-old girl and in a 5-year-old boy. Both showed the diagnostic criteria of hypoplastic anemia, skeletal deformities, and abnormal pigmentation. Hemorrhages and anemia were the presenting and outstanding symptoms and were the features that governed management. Although the bleeding and clotting times remained normal, the

platelet counts were invariably diminished. The megakaryocytes were so reduced in number that differential counts were not practicable. The erythrocytes were macrocytic with marked anisocytosis and polychromasia. On no occasion was the reticulocyte count raised in the boy but in the girl a reticulocytosis varying between 1.8% and 6.8% was present. There was no erythroid hyperplasia in the boy, nor on the first examination of the girl. The second examination of the girl showed evidence of erythroid activity. Evidence of hemolysis in vivo, as judged by splenomegaly, reticulocytosis, and raised serum bilirubin, was lacking. It was, nevertheless, decided to carry out a splenectomy, since the bone marrow was merely hypoplastic as judged by the specimens taken and not completely aplastic, a difference in degree that is held by some workers to be important in determining the effect of splenectomy. In the case of the girl there was an apparent improvement after splenectomy, but this was not maintained and it could be argued that this was but part of the natural history of the disease rather than a response to the splenectomy. In the boy, the platelet count rose on the second day after splenectomy but thereafter fell rapidly, and the patient died on the ninth postoperative day. In only two of seven cases of Fanconi's syndrome collected from the literature did the patients improve after splenectomy. The operation may be beneficial in patients with evidence of regenerative activity as demonstrated by the presence of erythroid hyperplasia of the bone marrow and reticulocytosis. It is debatable whether the inconvenience and risk of surgical intervention even in suitable cases are warranted by the sometimes longer benefit after splenectomy, the advantage of which, with modern techniques and safety of transfusion, is small. Splenectomy brings no improvement in those patients who do not show evidence of regenerative activity and in whom the reticulocyte count is not raised. Since other forms of treatment, such as liver extracts, folic acid, iron compounds, and cortisone, are without effect, reliance should be placed on repeated blood transfusions as the mainstay of therapy.

Epidemiological Evaluation of a Non-Cellular Pertussis Antigen. H. M. Felton and W. F. Verwey. Pediatrics **16:**637-651 (Nov.) 1955 [Springfield, Ill.].

There is a definite need for a less toxic pertussis immunizing agent. A noncellular antigen was first developed in 1951, prepared by treating sonic supernatants of Hemophilus pertussis cells with alcohol followed by precipitation with alum and dilution to proper potency with a thimerosal buffer. Statistical analysis of data from 197 children completely immunized with the noncellular antigen, 207 completely immunized with whole organism vaccine, and 238 nonimmunized control children suggested the following conclusions. The noncellular antigen can produce a satisfactory level of immunity to pertussis, as seen from the epidemiological data. The significantly higher agglutinin titers and better protection in humans suggest that there is a better response to the noncellular antigen than to the control vaccine even though mouse protective activities were about equal. The noncellular agent caused a febrile reaction of shorter duration than the control vaccine; there were also other indications that the former is less toxic. The frequency of pertussis cases in both immunized groups was significantly lower than in the nonimmunized control group.

THERAPEUTICS

Testicular Cancer: Management of Metastases, with Report of a New Chemotherapeutic Agent. O. Wildermuth. Radiology **65:** 599-603 (Oct.) 1955 [Syracuse, N. Y.].

Ninety-nine patients with testicular tumor were observed at the Tumor Institute of the Swedish Hospital in Seattle since 1935. Seventy-seven of these received treatment. The treated cases fall into two groups: those treated prior to 1946 and those treated subsequently. In the earlier period the practice was orchiectomy, with irradiation only for recurrences and metastases. Since then it has been the practice to follow orchiectomy by irradiation in all cases, even if there were no clinical signs of metastases. The results obtained have justified this combined therapy. The cure rate was 8.3% in the group of patients with metastases and 84% in those without metastases. Since the radiologist is often the first to observe the follow-up chest film blotched with disseminated metastases of testicular cancer, the author feels that they should know about the destructive effect exerted by nitrofurazone on such metastases. Furadantin, a related drug, is a urinary antiseptic that, when used internally, was observed to produce testicular atrophy. It was this effect that led to a trial of the drug in tumors of the testicle originating in the seminiferous epithelium. The author reports a patient who had been given postorchiectomy irradiation totaling 3,500 r throughout the midabdomen and pelvis. He was originally considered free of chest metastases, but restudy of the pretreatment films demonstrated early involvement. After two weeks, during which he received 21 gm. of nitrofurazone, there was a general systemic improvement, with softening of painful bilateral gynecomastia. The dosage of the drug was increased to 2 gm. daily, but two weeks and 28 gm. later, treatment had to be terminated because of severely painful peripheral neuropathy. The neuritis improved after three weeks, and treatment with nitrofurazone in daily doses of 1.5 gm. was resumed. The severe neuritis required the use of narcotics and finally nerve blocks, but roentgenologic evidence of metastases disappeared; the patient was able to resume his occupation two months later. He gained strength and weight and is still free from evidence of recurrence 18 months later.

Jaundice in Relation to Chlorpromazine Therapy. B. Isaacs, J. G. Macarthur and R. M. Taylor. Brit. M. J. **2:**1122-1124 (Nov. 5) 1955 [London, England].

Jaundice occurred in 3 of 26 patients between the ages of 8 and 65 years who were given 25 mg. of chlorpromazine three times daily for one week for the prevention and treatment of nausea and vomiting. A fourth patient with jaundice occurring in the course of treatment with chlorpromazine was referred to the authors from a psychiatric unit. The clinical features of these four patients were analyzed together with those of 39 additional patients in whom jaundice developed in the course of treatment with chlorpromazine and from whom information was obtained by questionnaire. The incidence of jaundice in chlorpromazine therapy was about 1%. Jaundice was more common in female than in male patients but bore no relation to the dose and duration of therapy. Jaundice varied in severity from mild and transient to severe, prolonged, and occasionally fatal illness. It is advised that chlorpromazine therapy be avoided when infective hepatitis is endemic, in the presence of liver disease, in malnourished patients, when other potentially hepatotoxic agents have been used, and when estrogens have been given. Should a febrile illness occur in the course of chlorpromazine therapy, evidence of liver damage should be sought. If it is found, chlorpromazine and all other drugs should be withdrawn and a high-protein, high-caloric diet given.

Treatment and Prevention of Hypertension and Its Cerebral Complications by Total Extract of Morinda Citrifolia Root. Dang Van Ho. Presse méd. **63:**1478 (Nov. 2) 1955 (In French) [Paris, France].

Seventy patients with benign hypertension were treated with total extract of the root of Morinda citrifolia. Fifty-eight of them obtained a favorable result within a period ranging from 10 to 70 days: their blood pressure level decreased from 20 to 70 mm. Hg, their general condition was improved, and their subjective symptoms disappeared. Thus, good results were obtained in 81%. Most of the patients had received prior treatment; the six who had not were the easiest to treat successfully. Three cases of particular interest are described, which clearly demonstrate the three essential properties of Morinda citrifolia. 1. The drug's hypotensive action is probably similar to that of Rauwolfia serpentina, but different from the usual hypotensors, including the ganglioplegics. Its effects are slow to manifest themselves and probably are obtained indirectly through slow and progressive improvement in the state of the arteriovenous system and the supporting connective tissue. 2. Morinda calms the sympathetic nervous system. Of all the symptoms of hyper-

tension, those connected with the sympathetic system are the first to be benefited by the drug. 3. The anticongestive property of Morinda was shown in its beneficial action on hemorrhoids, nasal congestion, and cerebral hemorrhage. The drug has other good qualities that will doubtless render it of value in the treatment of other conditions besides hypertension. The author has observed not one single case of intolerance.

Pulmonary Infiltration with Eosinophilia During Isoniazid Treatment. P. Perreau, M. Fresnau, B. Boumard and Y. Le Brizaut. Presse méd. **63:**1454-1456 (Oct. 29) 1955 (In French) [Paris, France].

The authors report two cases of labile pulmonary infiltration with eosinophilia in patients with tuberculous meningitis that was being treated with isoniazid. One patient was a 30-year-old woman in the eighth month of her second pregnancy, and the other a 5-year-old boy. Treatment had continued uneventfully over a period of several months before the appearance of the reactions, the drug being administered orally in doses of 5 mg. per kilogram. The infiltrate made its appearance several weeks after elevated doses had been started, that is, 20 mg. per kilogram. It was accompanied in both cases by digestive and blood disturbances of the kind seen in other patients treated with high doses of isoniazid, which fact suggests that drug intoxication was the cause of the pulmonary infiltration with eosinophilia.

A New Antituberculous Chemotherapeutic Agent: Cyanacetic Acid Hydrazide: Clinical Studies in Patients with Pulmonary Tuberculosis. M. Serembe. Minerva med. **46:**462-468 (Sept. 1) 1955 (In Italian) [Turin, Italy].

Cyanacetic acid hydrazide given to 40 men with various forms of pulmonary tuberculosis, in some of whom streptomycin, aminosalicylic acid, and isoniazid had been of little avail, while in others the administration of these drugs had to be suspended, proved to be about three times less toxic than isoniazid. It diffused rapidly into the organs and their fluids and reached concentrations that were much higher than those obtained with the standard antituberculous drugs. The patients, in whom all specific treatment was suspended a few days before the new therapy was started, received 250 to 600 mg. of the drug daily in divided doses of 50 mg. tablets five to six times during the day. The therapy was continued for from 30 to 120 days, and the total doses varied from 2 to 60 gm. The drug was well tolerated even by those patients to whom the administration of other drugs had to be discontinued. Irritability, paresthesia, headache, hyperreflexia, insomnia, and gastric and intestinal disturbances were not noted. The patients' appetite, with a consequent gain in body weight, and their sense of well-being were improved; cough decreased and often disappeared, especially in patients with exudative tuberculous forms and acute forms. During the first months of treatment, the sputum decreased in quantity, was more serous and more fluid, and became negative in 14 patients. Fever decreased and temperature was restored to normal; the objective chest symptoms improved in 30% of the patients; and the erythrocyte sedimentation rate decreased progressively in patients in whom the disease was of recent onset but remained practically unchanged in those with chronic forms. The best roentgenographic changes were seen in 15 patients with exudative tuberculosis in whom the exudative lesions regressed or became sclerotic. Active nodular processes also became sclerotic, and cavities decreased in size and sometimes, though rarely, disappeared in patients with cavitary tuberculosis. The action of the drug was slight on chronic lesions on which other antituberculous drugs had been of little avail. Marked improvement was seen in one patient with chronic tuberculosis and bilateral fibroulcerative bronchopneumonia of seven years' duration to whom the administration of other drugs had to be discontinued because of marked side-effects. Because these good results were obtained with cyanacetic acid hydrazide alone, it is assumed that even better results may be obtained by combining this new drug with streptomycin, aminosalicylic acid, or isoniazid. Studies are in progress to test this assumption and also the eventual development of bacterial resistance to cyanacetic acid hydrazide.

PATHOLOGY

Pulmonary Microlithiasis: Microlithiasis Alveolaris Pulmonum. G. Kent, E. S. Gilbert and H. H. Meyer. A. M. A. Arch. Path. **60:**556-562 (Nov.) 1955 [Chicago].

The essential feature of pulmonary microlithiasis is a striking radiographic opacity that resembles miliary tuberculosis but is accompanied by an almost complete absence of symptoms. This radiological appearance is produced by innumerable intra-alveolar "calculi," called corpora amylacea in the earliest reports, throughout the lung. A total of 14 cases, all in the European literature, have been found since 1856 when the first case report was published. An additional case, the clinical aspects of which are to be discussed elsewhere, was discovered on routine chest roentgenologic examination of a 35-year-old white man, otherwise perfectly well, who was hospitalized for excessive alcohol intake. A diagnosis of miliary tuberculosis was made, and he was transferred to a sanatorium where he was given combined chemotherapy. He left the sanatorium after four months. He was seen by a field nurse a few months later, and in February, 1955, he was admitted to the Chicago Municipal Tuberculosis Sanitarium. Prolonged intermittent exposure to mineral and cotton and wool dusts was disclosed in the history. The physical findings were negative. Study of a lung specimen $2\times2\times1$ cm. obtained at biopsy showed that the normal pulmonary architecture was obscured by innumerable barely visible gray or yellow nodules. Concretions morphologically similar to corpora amylacea, ranging in diameter from 0.02 to 0.3 mm., were found in some one-third of the alveoli. These concretions, however, differed from corpora amylacea as usually described in the following respects: 1. The amyloid stains were uniformly negative. 2. The concretions contained doubly refractile lipids. 3. Structurally, they were more irregular. 4. They were diffuse and occurred in areas not apparently the seat of previous pathological change. 5. They were heavily calcified. The first four of these differences are compatible with unusual variants of corpora amylacea and, as for the fifth, corpora amylacea are known to undergo calcification at times in the prostate and the lung. The concretions, therefore, may have been calcified corpora amylacea or they may at least have been formed by a similar process. Not enough tissue was removed to make chemical analysis possible, but the chemical composition of the concretions described in the literature seems to warrant the use of the term calculus, making the designation microlithiasis alveolaris pulmonum given to the condition by Puhr preferable to the original one of corpora amylacea. A common causative factor for the condition is not readily discernible in these cases, but its coexistence with rheumatic heart disease in two patients is especially interesting. Mitral stenosis may be associated with disseminated calcification and ossification of the lung, and in rheumatic pneumonitis the exudative fluid is rich in protein and frequently forms a thick eosinophilic lining referred to as hyaline membrane. The peculiar quality of this exudate, which is not easily reabsorbed, apparently lends itself to early organization and occasional calcification and ossification. Pulmonary microlithiasis may, therefore, be the result of an unusual exudative response to a variety of insults.

Absence of Pulmonary Artery with Compensating Bronchial Vascularization: Anatomic and Clinical Study. P. Broustet, R. Castaing, H. Bricaud and others. Presse méd. **63:**1342-1345 (Oct. 12) 1955 (In French) [Paris, France].

A 19-year-old girl died of cerebromeningeal hemorrhage. This patient had been given the diagnosis of tetralogy of Fallot with patent ductus arteriosus or bronchial arteries. Her only symptoms had been permanent cyanosis with superimposed paroxysms of cyanosis, and hippocratic fingers. Autopsy showed total absence of pulmonary artery, pulmonary vascularization being provided by three bronchial arteries issuing from the aorta; anomaly of lung segmentation, with two right lobes and one left lobe; an overriding aorta; a high interventricular septal defect; and bilateral cardiac hypertrophy. The association of the pulmonary malformations and the arterial anomalies is not a common one, and the authors found difficulty in classifying their case, which led them to review accepted systems of classification.

They finally concluded that absence of pulmonary artery is a definite entity that can be defined anatomically and embryologically and can serve as a basis for a logical classification of cases comprising this unusual feature. From the clinical point of view, there is very little difference between patients with severe atresia and those with absence of the pulmonary artery. The presence of a well-developed bronchial circulation may be accompanied on auscultation by a continuous murmur that is reinforced during systole and recalls that made by the ductus arteriosus. The slow progression of the condition and the long survival of patients with complete absence or severe atresia of the pulmonary artery make it difficult to decide whether to perform either a Blalock or Potts operation.

Pulmonary Alveolar Microlithiasis, or Calcinosis of the Lungs. T. L. Badger, L. Gottlieb and E. A. Gaensler. New England J. Med. **253:**709-715 (Oct. 27) 1955 [Boston].

A case of pulmonary alveolar microlithiasis, a rare disease in which microscopic stones are found within the pulmonary alveoli, is described in a man 45 years old, first seen because of abnormal pulmonary shadows on routine roentgenologic examination of the chest. At this time the patient was asymptomatic. Over the subsequent nine years of life, a slowly progressive dyspnea developed. For most of this time pulmonary function studies gave normal results. In the course of his disease the patient was seen by many clinicians and, although various diagnoses such as miliary tuberculosis, metastatic carcinoma, adenomatosis, and hemosiderosis were entertained, the correct diagnosis of calcinosis of the lung was made early on x-ray study which revealed a ground-glass appearance of both lung fields with minute particles of calcium densely demarcated in the walls of the alveoli. Microlithiasis as a diagnostic name was not considered, and the definitive diagnosis was made only after death. Multiple renal stones were passed by the patient during life, and pebbles were found in both kidneys at autopsy. Calcium salts had been deposited in the alveolar spaces of the lungs and in the kidneys, with relatively normal parenchyma in each organ. No calcium was found in the stomach walls. Chemical analysis of the ash obtained from a section of the right lower lobe of the lung revealed phosphorus pentoxide, 38.8%, calcium oxide, 51.8%, and ferric oxide, 0.1%. Extensive laboratory studies during life were negative. Ten similar cases were collected from the literature in which pathological and chemical findings agreed with those in the authors' case. It was Wells who in 1911 made the most searching investigation on the deposition of calcium salts in cartilage, in necrotic tissue, and especially in normal tissues. He emphasized the fact that all these calcium deposits have certain physicochemical properties in common but that physiological or metabolic alterations in the acid-base relation are most important for the chemical release and precipitation of calcium in all normal tissues, seen especially in the lungs, stomach, and kidneys. This metabolic concept of calcium deposits in normal tissues offers an explanation for the authors' case of pulmonary alveolar microlithiasis in which no other endocrine or pathological condition could be found to account for the calcium deposits in the pulmonary alveoli and in the kidneys.

RADIOLOGY

Contrasting Roentgenographic Pulmonary Patterns of the Hyaline Membrane and Fetal Aspiration Syndromes. H. G. Petterson Jr. and M. E. Pendleton. Am. J. Roentgenol. **74:**800-817 (Nov.) 1955 [Springfield, Ill.].

Of 188 newborn infants in whom a roentgenologic study of the lungs was carried out, 147 had respiratory distress and 41 were without clinical evidence of respiratory distress and served as controls. Thirty-seven of the 41 control infants showed prompt, uniform, and complete aeration of the lungs. The remaining four control infants showed fairly regularly aerated but not entirely clear lungs; all of these four infants were postmature with a gestation longer than 41 weeks. Three of them were meconium stained, and the fourth had evidence of fetal distress during labor. Of the 147 infants with respiratory distress, 138 showed one of two distinct abnormal roentogenographic pulmonary patterns. The more common quite uniform and finely reticulogranular pattern was presented by 104 infants, and the other nonuniform, coarse, and irregular pattern, by 34 infants. These two commonly observed abnormal roentgenographic patterns correlated well with two distinct syndromes, both clinically and pathologically. Of the 104 infants, 95 (more than 90%) were either premature or born by cesarean section, or both; these two principal clinical circumstances had been associated with hyaline membrane formation and resorption atelectasis by previous clinicopathological studies. Twenty-three of the 104 infants who showed this roentgenographic pattern and died within the period of their initial illness had diffuse hyaline membranes and alveolar atelectasis except for 2 infants in whom atelectasis was apparently prevented by inflammatory exudate. Thus the reticulogranular pattern appears to be the roentgenographic pattern associated with the hyaline membrane syndrome. In contrast, at least 28 of the 34 infants with the coarse, irregular roentgenographic pulmonary pattern were either postmature or meconium stained or both; these two principal clinical circumstances had been associated by previous studies with pathological evidence of aspirated amniotic sac contents (keratinized squamous cells or meconium) in the lungs with patchy atelectasis and emphysema, frequently with bleb formation. Four of the 34 infants with this roentgenographic pattern died and presented these pathological characteristics in their lungs. The coarse irregular pattern, therefore, has been interpreted as that pattern associated with fetal aspiration and the postmaturity syndrome. Neither pattern excludes the presence of pneumonia or intrapulmonary hemorrhage. It is proposed that the exceptional correlation of the patterns establishes roentgenographic examination as a reliable and valuable diagnostic and analytic aid in the care and study of newborn infants with pulmonary disease.

A Roentgenologic Study of a Human Population Exposed to High-Fluoride Domestic Water: A 10-Year Study. N. C. Leone, C. A. Stevenson, T. F. Hilbish and M. C. Sosman. Am. J. Roentgenol. **74:**874-885 (Nov.) 1955 [Springfield, Ill.].

Roentgenograms were made and repeated with matching views 10 years later in 237 persons, 116 of whom were residing in a high-fluoride area in Texas with 8 ppm of fluoride in drinking water, and the other 121 residing in a control area, where the water supply contained 0.4 ppm of fluoride. The following types of roentgenographic bone conditions were seen in human residents of the high-fluoride area who used the water supply containing 8 ppm fluoride for long periods: (1) increased bone density with or without coarsened trabeculation, with a "ground-glass" appearance; (2) coarsened trabeculation, showing lines of stress, without increased bone density; and (3) increased thickening of cortical bone and periosteum with equivocal narrowing of bone marrow spaces. Roentgenographic bone changes in varying degrees were observed in the first roentgenograms of 16 of the residents in the high-fluoride area. Ten years later 9 of the 16 showed no further bone change, 4 showed an increase in bone density, and 3 a decrease in density toward a normal appearance. Only one new case of increased bone density was recorded at the second roentgenologic examination. Statistical data presented in an earlier paper clearly demonstrated that except for dental mottling ingestion of water containing fluorides up to 8 ppm produces no deleterious bone changes. In the residents of the authors' control area there were four cases of increased density, two cases of increased coarsened trabeculation, and eight new cases of osteoporosis during the 10 year period, as compared with one new case of osteoporosis in the high-fluoride area. Increased bone density occurred predominantly in persons over 45 years of age. The authors' data suggest that excessive fluorides in a water supply may produce roentgenographic evidence of bone changes, but the observable changes occur in only 10 to 15% of those exposed. The bone changes are slight, often difficult to recognize, and in most cases equivocal in degree. They bear no resemblance to the bizarre findings described in some cases of long exposure to cryolite or rock phosphate dust nor to those attributed by some investigators to excessive fluorides in domestic water supplies. They are not associated with other physical findings, except for dental mottling in persons who

resided in the high-fluoride area during the tooth formative period up to 8 years of age. These bone changes cannot be definitely ascribed to excessive fluorides alone and they do not necessarily occur, even though the fluoride content of the bone may be six times that of normal bone. There is some indication that the ingestion of excessive fluoride in water and the "fluoride effect" of the degree observed in the authors' study may, on occasion, have a beneficial effect in adult bone, as in counteracting the osteoporotic changes of the aged.

ANESTHESIA

Anesthesia in Patients with Angina Pectoris and Cardiac Infarct of Old or Recent Onset Submitted to a New Intervention for Revascularization of the Myocardium by Ligation of the Internal Mammary Arteries. G. Muzzulini. Minerva chir. **10**:909-914 (Sept. 15) 1955 (In Italian) [Turin, Italy].

The author describes his method of inducing general anesthesia in patients with angina pectoris in whom ligation of the two internal mammary arteries at the second intercostal space was carried out on the basis that the ligation of these two arteries creates hypertension in the area of the two vessels and thus favors a better blood flow to the heart through the anastomoses present in the subserous stratum of the visceral and parietal pericardium and the base of the heart between the arterial coronary area and that of the internal mammary arteries. Because of the condition of these patients the anesthetic risk in them is much greater than the operative. A good general anesthesia should (1) guarantee excellent oxygenation of the patient; (2) influence as little as possible the preoperative arterial pressure values; (3) be nontoxic for the cardiac fibers and not influence the rhythm; and (4) be accepted by the patient so as to prevent the onset of circulatory disturbances in the hours preceding the intervention. Repeated large or small doses of Nembutal, depending on the patients' blood pressure, were given orally during the night preceding and on the morning of the operation to 15 patients with angina pectoris, four of whom had suffered a myocardial infarct 20, 6, 4, and 2 days earlier. The first dose was generally potentiated with 50 mg. of an antihistaminic preparation (Fargan) given subcutaneously. The last dose of the barbiturate was given two hours before anesthesia was induced, at which time a synthetic preparation (Dromoran) was also given instead of morphine, which seemed to depress the respiration too much, and it was combined with 0.5 mg. of atropine and 50 mg. of Fargan. With this premedication the patient is conscious but drowsy and indifferent at the time anesthesia is to be induced and his arterial pressure is unchanged. Anesthesia is induced slowly, progressively, with very small doses of a slow-acting barbiturate that has a slight depressing action on respiration. The usual variations in arterial pressure that follow the induction of anesthesia by means of barbiturates are thus prevented. Patients who were forced to maintain a sitting position were anesthetized in that position and made to lie down only after they had become unconscious. As soon as the patient was unconscious he was brought to the operating room and closed-circuit oxygenation was instituted. All the patients tolerated the intervention well; the use of analeptics and heart tonics was never necessary; and the pressure values remained practically unchanged during the intervention. These results show that it is possible to induce general anesthesia safely in patients with angina pectoris and cardiac infarct, provided a good oxygenation of the heart fiber is secured and the preoperative arterial pressure is maintained.

Alcohol Inhalation in the Treatment of Acute Pulmonary Edema in the Immediate Postoperative Period. R. Weyl. Illinois M. J. **108**:265-269 (Nov.) 1955 [Chicago].

Fairly large amounts of fluid can be tolerated in the respiratory passages as long as no foam is formed. The foam increases the volume of the air-fluid mixture, and the modified physical properties of the fluid block the small bronchi. Anoxia develops and is followed by higher pressure in the pulmonary artery and increased permeability. This is why it occurred to Luisada that, if an antifoaming agent could modify the surface tension in such a way as to decrease the foam, oxygen could get through and the vicious circle would be interrupted. Antifoaming agents, particularly alcohols, were tested in a series of experiments. The histories of seven patients are reported, in whom acute fulminating edema developed in the immediate postoperative period, and who were treated with alcohol inhalation. Three patients had suffered acute myocardial infarcts; two patients were operated upon for mitral stenosis; one incident happened after resuscitation for cardiac arrest and one was due to respiratory obstruction. In all seven patients the response to the treatment seemed dramatic, the outpour of foam stopped, the color improved, and the acute suffocation due to oxygen want could be avoided. All seven patients were receiving oxygen when the pulmonary edema started; therefore, the success of the therapy seems to be attributable to the antifoaming action of the alcohol. There were no fatalities during the attack in this series. Four of these patients left the hospital in good condition; one patient did well for another six weeks, and two patients died within three days after surgery, one of fulminant peritonitis, the other of cerebral edema. Discussing the technique, the author says that the wick-type ether vaporizer on the anesthesia machine was emptied of ether, the wick dried, and the jar filled with 95% alcohol. Oxygen was used for vaporization and the vaporizer was opened to full capacity. The closed circle absorption technique was used to be able to assist breathing whenever necessary. Thus when pulmonary edema started in the operating room, the equipment and the 95% alcohol were there, and alcohol inhalation could be started immediately. For the two patients in whom the pulmonary edema occurred when they were already in the recovery room, the standard equipment for use on the floors was available. The success obtained seems to be due to the early onset of treatment. Since there seems to be no contraindication to the use of alcohol vapor inhalation and since it can be combined with any other treatment, it is recommended to use alcohol vapor inhalation during surgery or in the immediate postoperative period whenever there is pulmonary edema and even when there is only a suspicion of beginning pulmonary edema.

PUBLIC HEALTH

Emergency Handling of Frozen Foods. J. B. Hozier and James A. Anderegg. Pub. Health Rep. **70**:1045-1048 (Nov.) 1955 [Washington, D. C.].

With the great expansion of the frozen food industry during the past decade, the emergency handling of frozen foods has become increasingly important. Failure of electric power occurs frequently as a result of natural disasters. Among the many factors that determine the length of time frozen foods can be kept without spoiling during a power failure in either a home freezer or a commercial warehouse are: (1) type, quantity, and condition of the insulation of the freezer or warehouse; (2) temperature within the freezer or warehouse at the time of power failure (the colder the food, the longer it will stay frozen); (3) type of products stored (frozen meats, for example, will absorb heat much more slowly than frozen baked foods); (4) how full the freezer or warehouse is at the time of power failure, as generally a full freezer will hold frozen foods hours longer than an almost empty one, and (5) whether or not it becomes necessary to open a freezer or warehouse. The latter is the most important of all the factors influencing holding time. Once power has stopped, frozen food storage units should not be opened except to transfer the food elsewhere or to add dry ice. When available, dry ice is the best deterrent to temperature rise, particularly in home freezers. Despite the heavy loss of food in New England as a result of Hurricane Carol, considerable quantities of frozen foods that otherwise might have spoiled were preserved with dry ice flown in from communities not affected by the storm. Because of the rupture of cellular structure during freezing, foods that have been frozen deteriorate much more rapidly after thawing than do fresh foods. Almost any method of preserving fresh food—canning, cooking, salting, smoking—can be used to preserve food that has been frozen.

BOOK REVIEWS

Allergy Cooking: A Guide with Menus and Recipes. By Marion L. Conrad. Foreword by David Leonard Lieberman, M.D. Cloth. $5. Pp. 380. Thomas Y. Crowell Company, 432 Fourth Ave., New York 16, 1955.

When a physician prescribes changes in a patient's food habits, the patient's troubles have just begun. He needs practical help in carrying out the physician's orders and especially in avoiding the many pitfalls awaiting him. Mrs. Conrad, a home economist experienced in providing suitable food for her own family of food allergy sufferers, offers just this assistance. This book contains over 600 easy-to-prepare recipes and menus suitable for diets that must exclude even such staple foods as milk and milk products, eggs, and wheat and other cereals. In addition she has discussed all kinds of foods, such as meats, fish, poultry, fruits, vegetables, and candies, in relation to the various types of food allergies. The author emphasizes that no one food is indispensable. She has designed the book to supplement, not to supplant, proper medical guidance.

Preventive Medicine in World War II. Volume II: Environmental Hygiene. Editor-in-chief: Colonel John Boyd Coates, Jr. Editor for preventive medicine: Ebbe Curtis Hoff, M.D., Ph.D., Assistant editors: Phebe M. Hoff, M.A., Audrey A. Bill, M.D., Dr.P.H. Publications editor: Gertrude G. Johnson, Medical Department, United States Army, Office of Surgeon General, Department of Army. This volume was prepared for publication in Historical Unit, Army Medical Service. Cloth. $3.50. Pp. 404, with 25 illustrations. Superintendent of Documents, Government Printing Office, Washington 25, D. C., 1955.

This volume on environmental hygiene is one of several to be published concerning preventive medicine as a part of the history of the medical department of the U. S. Army in World War II. While it is an account of the part the medical department played in this field, other branches of the armed forces and various federal agencies were also involved. Here are recorded those plans, operations, and activities that used, modified, and controlled environment for health purposes. The scope of the problem was global. However, no attempt is made to chronicle the details of the practice of environmental hygiene by theaters of war. The subjects with which this volume is concerned are water purification, control of insects, disposal of waste, housing, rodent control, and foreign quarantine. Each chapter has its own author. A contract was drawn up between the Army Medical Library and the Medical College of Virginia to establish an editorial office from which contact was made with the authors. The manuscripts then were submitted to the editor-in-chief of the history of the medical department in World War II for final editing and processing for publication.

Some interesting facts are stated. For example, no plague was reported among U. S. military personnel, and no plague-infecting rodent was ever recovered from a U. S. military vessel or aircraft. Although parts of our Army operated in officially declared areas of cholera, only 13 cases appeared among all U. S. Army personnel. There were only 102 cases, none fatal, of louse-borne typhus, and some of those were among research personnel who were exposed far in excess of the average person. No case of yellow fever was incurred by U. S. Army personnel in any area. Concerning the spread of agricultural pests during World War II, 13 insects were newly reported in Hawaii and were apparently introduced there from the United States and from the south and southwest Pacific, and of these at least two, it was considered, would probably prove of economic advantage rather than harm. Several of the remainder were definitely harmful insects. Australia, before the war, forbade the importation of fresh pork, but later it was agreed that pork might be imported by American forces provided the refuse was incinerated. The Australians eventually insisted that this requirement be modified to provide that refuse be merely heat-treated, thus permitting the use of it for feeding and rendering. This procedure was difficult to carry out properly, and so hog cholera developed in Australia, and the killing of thousands of animals was required before it could be controlled. On the whole, the Army program of quarantine clearance in transport operations by water and air was effective, although not perfect. The principles and techniques thus evolved should prove of value in peacetime civil quarantine of commercial traffic and in case there should be another war.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Atlas of Clinical Pathology of the Oral Mucous Membrane (a Practical Approach to Diagnosis). By Balint J. Orban, M.D., D.D.S., Professor of Periodontics, Loyola University School of Dentistry, Chicago; Frank M. Wentz, D.D.S., M.S., Ph.D., Associate Professor of Periodontics, Loyola University School of Dentistry; and contributors. Cloth. $12.50. Pp. 135, with 214 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1955.

The aim of this book is to present a concise atlas of clinical pathology of the oral mucosa that will incorporate a practical approach to the diagnosis of oral lesions. The material is classified according to etiology and pathological tissue changes, and every disease is illustrated by a picture in color. The oral diseases are summarized under these headings: clinical feature, course of the disease, differential diagnosis, frequency, and therapy. Clinical pictures are followed by histopathological descriptions of the lesions. Without attempting to compete with older, bulkier textbooks, this atlas should find a useful place in the physician's library for quick, helpful reference.

Introduction to Virology. By Gilbert Dalldorf, Director, Division of Laboratories and Research, New York State Department of Health, Albany. Cloth. $3.50. Pp. 102, with 6 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1955.

This well-organized booklet, which is based on lectures and laboratory exercises in a medical school, presents concisely the aspects of virology that are of major interest to physicians. It serves as an excellent introduction into this rapidly expanding field. The first short chapter defines the nature of viruses and viral diseases. This is followed by short descriptions of the clinical and laboratory aspects of the different viral diseases. The final part of the book deals with technical matters, presenting a useful description of the virus laboratory and a somewhat sketchy delineation of the common techniques in virology. The presentation is didactic but easy to comprehend, and the great amount of information compressed into this small, readable book is surprising. It can be highly recommended for medical students or for practitioners trying to obtain initial information about this field of medicine.

The Relief of Symptoms. By Walter Modell, M.D., F.A.C.P., Associate Professor, Clinical Pharmacology, Cornell University Medical College, New York. Cloth. $8. Pp. 450. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C. 2, England, 1955.

Much of the energy of practicing clinicians is focused on the problem of curing disease; less attention is directed to the problem of relieving distress. This book, which is offered as a practical guide for the relief of symptoms, is the culmination of the author's philosophy that to ignore the reactions of patients to distress is to deprive them in great measure of what current medical therapy can accomplish. Twenty-four chapters of the book are devoted to as many symptoms, covering at least 95% of those complaints that bring patients to the doctor's office. Such common symptoms as pain, insomnia, constipation, loss of appetite, palpitation, cough, fever, vertigo, jaundice, convulsions, frequency of urination, anxiety, and unconsciousness are included. Five introductory chapters are devoted to the significance of symptoms, their analysis, their importance, the methods of providing relief, and the analysis of response to treatment. This book presents a highly readable and informative case for symptomatic medicine and is warmly recommended for a younger generation of practicing clinicians.

QUERIES AND MINOR NOTES

LEUKEMIA FOLLOWING IRRADIATION

To the Editor:—*Is there any proof that exposure to irradiation, such as that experienced by workers in atomic energy plants, may be the cause of acute lymphatic leukemia? If so, how much irradiation is likely to cause such a lesion?*

M.D., Missouri.

Answer.—There is no scientific proof to support the idea that leukemia is more frequently encountered in persons exposed to low levels of ionizing radiation in the range of the "maximum permissible levels," which are those generally observed in atomic energy plants, than in the general population. In published studies correlating increased incidence of human leukemia with exposure to ionizing radiation, exposures have in general been probably rather large. There is a great deal of experimental evidence that ionizing radiation is leukemogenic in animals and a considerable amount of evidence that leukemia is more frequent in human beings exposed to large amounts of radiation. Henshaw and Hawkins (Incidence of Leukemia in Physicians, *J. Nat. Cancer Inst.* **4**:339, 1944) recognized leukemia to be about 1.7 times as frequent in physicians as among white males in the general population. March (Leukemia in Radiologists, *Radiology* **43**:275, 1944; Leukemia in Radiologists in a 20 Year Period, *Am. J. M. Sc.* **220**:282, 1950) compared the incidence of leukemia in radiologists and in physicians who were not radiologists and concluded from a comparison of mortality statistics that leukemia occurred more than nine times as frequently in radiologists as in nonradiologist physicians. The incidence of leukemia has also been studied in survivors of the atomic bombings in Japan. Folley and co-workers (Incidence of Leukemia in Survivors of the Atomic Bomb in Hiroshima and Nagasaki, Japan, *Am. J. Med.* **13**:311, 1952) concluded that there was a significant increase in the incidence of leukemia in the exposed survivors of the bombings as compared to the nonexposed populations in Hiroshima and Nagasaki. A more recent statistical analysis of the incidence of leukemia among 98,000 survivors of the Hiroshima bombing, made by Moloney and Kastenbaum (Leukemogenic Effects of Ionizing Radiation on Atomic Bomb Survivors in Hiroshima City, *Science* **121**:308, 1955), showed that the 50 verified cases of leukemia were distributed in such fashion as to demonstrate a significant increased incidence among exposed survivors in comparison to those unexposed survivors. There is then reason to believe from statistical evidence that large doses of ionizing radiation may be leukemogenic in man, but this action has not been demonstrated with low levels of exposure.

NASAL SURGERY FOLLOWING FACIAL INJURIES

To the Editor:—*When a 55-year-old man sustained severe facial bone fractures three months ago, a flow of cerebrospinal fluid was noted from the nose. He has made a good recovery, but he has a badly deviated septum that requires a submucous resection. Because of the fact that the cribriform plate was probably fractured at the time of his accident, how long would you wait before performing the submucous resection?*

Orel Friedman, M.D., Glens Falls, N. Y.

Answer.—It would be wise to wait a minimum of nine months from the time of original injury before undertaking nasal surgery. In contemplating this surgery one must recognize the possibility that the previously fractured cribriform plate area may have healed by fibrous rather than bony union and that even mild trauma might result in refracture with recurrence of cerebrospinal rhinorrhea. For this reason, particular caution should be taken in dealing with the perpendicular plate of the ethmoid during surgery. Any rocking or twisting motion of bony parts should be avoided. Rather, the bony obstruction should be removed by gentle-acting biting forceps. In this situation one would do well to use the minimum amount of packing of the nasal chambers following surgery. The preoperative and postoperative administration of antibiotics would be indicated.

STRONGYLOIDES STERCORALIS INFESTATION

To the Editor:—*An obese, 57-year-old man in apparent good health awoke at 2 a. m. with intense pain over the entire abdomen with board-like rigidity. He was given 1/32 grain (1.6 mg.) of Dilaudid, but his pains continued severe, and, rapidly going into a state of shock within an hour after onset, he was given 1/16 grain (3.8 mg.) of Dilaudid and 1/150 grain (0.4 mg.) of Atropine and rushed to the hospital. A leukocyte test and differential count showed 19,000 white blood cells per cubic millimeter, 85% polymorphonuclear cells, 9 eosinophils, and 6 lymphocytes, which seemed a definite indication for an exploratory operation. However, before the blood cell count could be completed his pain disappeared along with the board-like rigidity of his abdomen and he seemed to be entirely comfortable with only some localized tenderness in the lower right quadrant. There had been no fever or vomiting. A stool examination was made for fat and amylase along with a microscopic examination that showed an overwhelming infestation with Strongyloides stercoralis. He has been given two treatments with piperazine (Antepar) citrate and two treatments with gentian violet and is now taking Antepar and sulfasuxadine with apparently no effect on this particular parasite. Is there a specific treatment for this parasitic infestation? The patient is continuing in apparent good health, but, of course, he wishes to be relieved of the intestinal parasite.*

H. D. Allen Jr., M.D., Milledgeville, Ga.

Answer.—At present there is no specific treatment for Strongyloides stercoralis infections. In critical tests, piperazine citrate has not proved to be of any value, as have other drugs, including Hetrazan (1-diethylcarbamyl-4-methyl piperazine dihydrogen citrate). Gentian violet NNR has been employed to a greater extent than any other drug. However, it seems to lack value in many cases. Transduodenal intubation with 25 cc. of a 1% solution of gentian violet has also been employed but with no great success. Palmer (*Am. J. Trop. Med* **30**:91-92 [Jan.] 1950) reported good therapeutic response with intravenous injections of 20 cc. of an 0.5% solution of gentian violet injected slowly, once a day for 20 days. No ill-effects were observed. However, Palmer has since informed this correspondent that subsequent to his publication he encountered reactions to the treatment and has abandoned its use. As of this writing, there is no known treatment that can be depended on to eradicate the infection.

RECURRING SORE THROAT

To the Editor:—*Kindly recommend prophylactic treatment of sore throat that occurs several times in winter only, accompanied by fever and a tendency to extend to the chest. The patient is a woman, aged 63, with a history 25 years ago of rheumatic spondylitis. Her tonsils have been removed. There is no sensitivity to chemotherapeutic drugs or to antibiotics.*

J. T. Brosnan, M.D., Chicago.

Answer.—The prophylaxis of the recurring sore throat depends on the cause. If the sore throat is due to group A hemolytic streptococci, penicillin (200,000 units) should be given orally every six hours for seven days each month from Septem-

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

ber to June. Penicillin has been shown to control group A streptococcic infections. In the absence of sulfonamide-resistant strains of streptococci, sulfadiazine, 0.5 to 1 gm. daily, from September to June may be used. Toxic effects as well as resistance of the streptococci is not uncommon with the sulfonamides. It is for this reason that penicillin is preferred to sulfadiazine.

PELVIC TUBERCULOSIS

To the Editor:—*Curettage in the course of a fertility study revealed endometrial granulomas suggestive of tuberculosis, and guinea pig inoculation of menses blood was reported positive of tuberculosis. The patient is asymptomatic, and x-rays of her chest are negative. A second purified protein derivative test was positive. Please advise management.*

M.D., Connecticut.

Answer.—There is no uniformity in the treatment of pelvic tuberculosis, but good results have been obtained with the combination of streptomycin and aminosalicylic acid (PAS) with or without the use of isonicotinic acid hydrazides. The following schedule is an excellent one: 1 gm. streptomycin three times a week given intramuscularly and 300 mg. isoniazid daily divided into three doses of 100 mg. This treatment should be given for four months. Another satisfactory treatment is: a single dose of 1 gm. streptomycin intramuscularly daily and 3 gm. PAS orally four times a day for at least two months. All the tests for tuberculosis should be repeated every 6 months because not infrequently there is a recurrence after 12 to 24 months. Even if the tuberculosis is apparently healed, the outlook for a baby is poor.

IMMUNITY TO POLIOMYELITIS CONFERRED TO INFANT

To the Editor:—*If a pregnant woman is given the Salk vaccine will it impart a small amount of immunity to the unborn child? If so, about how long would it be effective?*

Robert E. Garcia, M.D., Blythe, Calif.

Answer.—In the course of studies with poliomyelitis vaccine, over the past several years, there have been opportunities to inoculate young women either prior to or during pregnancy. From samples of cord blood thus made available when these women gave birth, it is known that there has been a transfer of maternal antibody. In none of these cases were observations made on the infant after birth, but it is an accepted fact that passively acquired maternal antibody persists for a period of approximately six months. There is no reason to expect that this would not be true in cases of poliomyelitis antibody, whether it be acquired by the mother as a result of natural infection or by vaccination.

OVULATION RARE AFTER LAST MENSTRUATION

To the Editor:—*A 47-year-old woman has had no menstrual periods for two years and had only rare menstrual periods for two years preceding that time. For the past two years she has continued to use a recommended contraceptive. She would like to know whether this method should be discontinued now and be assured she can no longer conceive children.*

M.D., Washington.

Answer.—The chances of this woman becoming pregnant are so rare that she may safely give up the use of contraceptives. Even if she should have a menstrual period, which is most unlikely, it would almost certainly be associated with absence of ovulation. Novak and Novak (Textbook of Gynecology, ed. 4, Baltimore, Williams and Wilkins Company, 1952, p. 123) say: "While ovulation rarely occurs after from six months to a year following the last menstruation, we have found a typical progestational endometrium six years after the menopause in one case, and in another fully ten years after x-ray induction of the menopause which had been done at the age of 46 because of functional bleeding. Such incidences, however, are exceedingly rare."

CHANGES IN PRESERVED BLOOD

To the Editor:—*Is there any deterioration in the hemoglobin, red blood cell mass, white blood cell mass, or differential count in preserving blood at icebox temperature for 48 hours? The blood is usually taken from the vein and put into a dried balance oxalate solution. It is then refrigerated over the weekend, and the blood cell count and sedimentation rate are done on Monday morning. Would there be any change in blood sugar level readings for specimens that are oxalated and preserved in sodium fluoride? Should there also be any change in the appearance of the leukocytes and erythrocytes when observed through the microscope on a stained smear?*

M.D., New Jersey.

Answer.—A blood specimen drawn into and mixed with the customary oxalate powder and subsequently stored in the refrigerator is satisfactory for hemoglobin level determination for 48 hours; however, the erythrocyte level tends to drop during this time and should be estimated no later than 24 hours after collection. Leukocytes deteriorate rapidly and are preferably estimated as quickly as possible after collection, certainly no longer than 24 hours. The sedimentation rate shifts toward the normal and should be determined within two hours following collection. In the presence of sodium fluoride, the blood sugar level determination would be unaltered by 48 hour storage; however, an oxalated specimen shows diminution in blood sugar level readings in a matter of hours, and tests on a 48-hour-old specimen would be unreliable. This consultant has had no experience with blood specimens containing both oxalate and sodium fluoride but would anticipate that readings would be satisfactory. The blood smear is satisfactory for staining 48 hours after blood collection if the blood elements are spread on the slide promptly after collection and dried before storage.

AIR CONDITIONER IN OPERATING ROOM

To the Editor:—*In the Queries and Minor Notes section in* The Journal, *Aug. 13, 1955, page 1405, is a discussion on air conditioners in operating rooms. The answer describes what may be termed a luxury installation for the operating room itself and a hazardous one for the conventional room conditioner. Horizontal separation affords little protection in a situation that also permits effective circulation of conditioned air. A correct and economical installation can be made in accord with section 3-2 (6) NFPA no. 56 "Recommended Safe Practice for Hospital Operating Rooms, March 1954," which states: "Window type re-circulating air conditioning units may be installed in exterior windows of anesthetizing locations. If installed, such units shall be provided with a gasketed metal divider interposed between non-ferrous fan blades (room side) and the fan motor (outside the room). Window sash shall tightly fit the gasketed divider. A manually operated fresh air intake port may be provided in the metal divider. Electrical controls and other electrical equipment for such units installed within anesthetizing locations (room side) shall comply with the requirements of Section 5-3 (a) or Section 5-3 (b)." Section 5-3 (a), "Fixed Installation—Hazardous Locations," states: "Electrical wiring and fixed equipment installed less than 5 feet above the floor of rooms used as anesthetizing locations (See Section 2-2) shall comply with the requirements of Class I, Group C, Division 1 locations of Article 500 of the National Electrical Code (explosion-proof)." Section 5-3 (b), "Fixed Installation—Ordinary Locations," states: "The standards of the National Electrical Code for ordinary locations shall be the minimum requirements for electrical wiring and fixed equipment installed more than 5 feet above the floor of rooms used as anesthetizing locations. In addition, devices, appliances, fixtures or equipment, if of a type incorporating sliding contacts arcing or sparking parts, including overcurrent protective devices, shall be of the totally enclosed type or shall have all openings guarded or screened so as to prevent the falling of hot particles."*

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